Description of Medication

Palivizumab is a humanized monoclonal antibody indicated for prevention of serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) in pediatric patients at high risk of RSV disease. Palivizumab works by exhibiting neutralizing and fusion-inhibitory activity against RSV; these activities inhibit RSV replication in laboratory and clinical studies.

Recommended Authorization Criteria

Coverage of palivizumab for prevention of RSV disease for the duration of one RSV season is recommended in those who meet one of the following criteria:

Food and Drug Administration (FDA)-Approved Indications

1. **RSV, Prevention in an Infant Born Prematurely.** Approve for a maximum of 5 months during the RSV season (lasting November through March in most areas) in children who meet the following criteria (a and b): [Example: If patient meets criteria in November, approve for 5 months; if patient meets criteria in December, approve for 4 months etc.]

   a) The infant is ≤ 12 months of age at the start of the RSV season; AND
   b) The infant was born before 29 weeks, 0 days gestation (≤28 weeks, 6 days gestation).

   Note: For children born during the RSV season, fewer than 5 monthly doses will be needed.

   Synagis is FDA-approved for the prevention of RSV infections in high-risk pediatric patients which includes infants born prematurely.\(^1\) 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 with Synagis are clear. For this reason, infants born at 29 weeks, 0 days’ gestation or later are not universally recommended to receive Synagis unless they meet other conditions of coverage (e.g., CHD or CLD). Synagis is not recommended in the second year of life on the basis of prematurity alone. There are some experts who believe that on the basis of the data quantifying a small
increase in the risk of hospitalization, even for infants born earlier than 29 weeks, 0 days gestation, Synagis prophylaxis is not justified.

2. **Respiratory Syncytial Virus (RSV), Prevention in an Infant with Chronic Lung Disease (CLD).** Approve for a maximum of 5 months during the RSV season (lasting November through March in most areas) in children who meet ONE of the following conditions (a or b).

   [**Example:** If patient meets criteria in November, approve for 5 months; if patient meets criteria in December, approve for 4 months etc.]

   a) Infants ≤ 1 year of age at the start of the RSV season must meet the following criteria (i and ii):
   
   i. The infant was born at < 32 weeks, 0 days gestation; AND
   
   ii. The infant required > 21% oxygen for at least 28 days after birth.

   OR

   b) Infants ≤ 2 years of age at the start of the RSV season must meet the following criteria (i, ii, and iii):

   i. The infant was born at < 32 weeks, 0 days gestation; AND
   
   ii. The infant required > 21% oxygen for at least 28 days after birth; AND
   
   iii. The child has required medical therapy (i.e., supplemental oxygen, diuretic therapy, or chronic corticosteroid therapy) during the 6 months before the start of the second RSV season.

Synagis is indicated for the prevention of RSV infections in high-risk pediatric patients which includes infants with CLD. The AAP guidelines (2014) recommend that prophylaxis be considered during the RSV season during the first year of life for preterm infants who develop CLD of prematurity defined as gestational age < 32 weeks, 0 days and have a requirement for > 21% oxygen for at least the first 28 days after birth. During the second year of life, consideration of Synagis is recommended only for infants who satisfy the definition of CLD detailed above 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. Most children who are hospitalized with RSV are ≤ 1 year of age and < 20% of all pediatric RSV hospitalizations occur during the second year of life. Regardless of the presence of absence of comorbidities, RSV hospitalization rates decline during the second RSV season for all children.

3. **RSV, Prevention in an Infant with Congenital Heart Disease (CHD).** Approve for a maximum of 5 months during the RSV season (lasting November thru March in most areas) in children who meet the following criteria (a, b and c): [**Example:** If patient meets criteria in November, approve for 4 months etc.]

   a) The infant is ≤ 1 year of age at the start of the RSV season; AND
   
   b) According to the prescribing physician, the infant meets one of the following conditions (i, ii, iii, or iv):

   i. The infant is considered to have hemodynamically significant cyanotic CHD; OR
   
   ii. The infant has acyanotic heart disease AND is receiving medication to control heart failure AND will require cardiac surgical procedures; OR
   
   iii. The infant has moderate to severe pulmonary hypertension; OR
   
   iv. The infant has lesions adequately corrected by surgery AND continues to require medication for their congestive heart failure; AND
   
   c) Synagis is prescribed by or in consultation with a cardiologist or intensivist.
Synagis is indicated for the prevention of RSV infections in high-risk pediatric patients which includes children with hemodynamically significant CHD. The AAP recommends use of prophylactic Synagis in children ≤ 1 year of age with hemodynamically significant CHD. Children with hemodynamically significant CHD who are most likely to benefit from immunoprophylaxis include infants with acyanotic heart disease who are receiving medication to control CHF and will require cardiac surgical procedures and infants with moderate to severe pulmonary hypertension. Decisions regarding prophylaxis for infants with cyanotic heart defects in the first year of life may be made in consultation with a pediatric cardiologist. The following groups of infants are not at increased risk for RSV infection and generally should not receive immunoprophylaxis: 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 lesions adequately corrected by surgery, unless they continue to require medication for CHF; 3) Infants with mild cardiomyopathy who are not receiving medical therapy for the condition and; 4) Children in the second year of life.

A retrospective analysis of children < 3 years in the Tennessee Medicaid program revealed that the RSV hospitalization rate for children with CHD in the second year of life (18.2/1,000) was less than half the hospitalization rate for low-risk infants in the first 5 months after birth (44.1/1,000), a group for whom Synagis prophylaxis is not recommended. Therefore, prophylaxis is not recommended during the second year of life.

**Other Uses with Supportive Evidence**

4. **RSV, Prevention in an Infant with Anatomic Pulmonary Abnormalities or a Neuromuscular Disorder.** Approve a maximum of 5 months during the RSV season (lasting November thru March in most areas) in children who meet the following criteria (a and b). [Example: If patient meets criteria in November, approve for 5 months; if patient meets criteria in December, approve for 4 months etc.]
   a) The infant is ≤ 1 year of age at the start of the RSV season; AND
   b) According to the prescribing physician, the patient’s condition compromises the handling of respiratory secretions.

The risk for hospitalization is not well defined in children with neuromuscular disorders that impair the ability to clear secretions from the upper airway because of ineffective cough, recurrent gastroesophageal tract reflux, pulmonary malformations, tracheoesophageal fistula, upper airway conditions, or conditions requiring tracheostomy. Infants with neuromuscular disease or congenital anomaly that impairs the ability to clear airway secretions from the upper airway because of ineffective cough are known to be at risk for a prolonged hospitalization related to lower respiratory tract infection and, therefore, may be considered for prophylaxis during the first year of life.

In the professional opinion of specialized physicians reviewing the data, children ≤ 1 year of age with an underlying condition that predisposes to respiratory complications are considered high-risk in the clinical practice setting and should receive Synagis.

5. **RSV, Prevention in an Immunocompromised Child.** Approve for a maximum of 5 months during the RSV season (lasting November through March in most areas) in children who meet the following criteria (a, b, and c): [Example: If patient meets criteria in November, approve for 5 months; if patient meets criteria in December, approve for 4 months etc.].
   a) The child is < 24 months of age at the start of the RSV season; AND
   b) Synagis is prescribed by or in consultation with an immunologist or infectious diseases specialist; AND
c) According to the prescribing physician, the child is/will be profoundly immunocompromised during the RSV season (e.g., receiving chemotherapy, transplant).

Guidelines note that there are no population-based data on the incidence of RSV hospitalization in children who undergo solid organ transplantation. Severe and even fatal disease attributed to RSV is recognized in children receiving chemotherapy because of other conditions, but the efficacy of prophylaxis in this cohort is not known. Prophylaxis may be considered for children < 24 months of age who are profoundly immunocompromised during the RSV season.10

In the professional opinion of specialist physicians reviewing the data, we have adopted this criterion.

6. RSV, Prevention in a Child with Cardiac Transplant. Approve for a maximum of 5 months during the RSV season (lasting November through March in most areas) in children who meet the following criteria (a, b, and c): [Example: If patient meets criteria in November, approve for 5 months; if patient meets criteria in December, approve for 4 months etc.]. Note: Children with cardiac transplant may also be immunocompromised. In children who do not meet criteria for cardiac transplant below, please see criterion 5 above.

a) The child is < 2 years of age at the start of the RSV season; AND
b) The child has undergone or will undergo cardiac transplantation during the current RSV season; AND
c) Synagis is prescribed by or in consultation is a cardiologist, intensivist, or transplant physician.

The AAP guidelines note that in children < 2 years of age who undergo cardiac transplantation during the RSV season may be considered for Synagis prophylaxis.10

Exclusions (Limitations)

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Synagis has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. RSV, Prevention in a Patient with Cystic Fibrosis (CF) Who Does Not Meet Any of the Approval Criteria Above. The AAP guidelines for RSV (2014) note that routine use of Synagis prophylaxis in patients with CF, including neonates diagnosed with CF by newborn screening, is not recommended unless other indications are present. An infant with CF with clinical evidence of CLD and/or nutritional compromise in the first year of life may be considered for infants 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 weight for length less than the 10th percentile. A Cochrane Review identified one trial (presented in poster/abstract form) eligible for their review of Synagis prophylaxis in children with cystic fibrosis.11 In this prospective, double-blind, placebo-controlled, multi-center study, 14.1% vs. 14.9% of Synagis and placebo-treated patients, respectively were hospitalized within the first 6 months, and only one patient in each group was identified with RSV infection. The authors calculated a risk ratio and found no significant difference between the two groups (risk ratio [RR] 1.02; 95% CI: 0.06, 16.09). There were no deaths in either group of patients during the first 6 months follow-up; this outcome was not reported at 12 months follow-up.
2. **RSV, Prevention in a Patient with Down Syndrome Who Does Not Meet Any of the Approval Criteria Above.** Limited data suggest a slight increase in RSV hospitalization rates among children with Down syndrome. However, data are insufficient to justify a recommendation for routine use of prophylaxis in children with Down syndrome unless qualifying heart disease, CLD, airway clearance issues, or prematurity is present. Multiple logistic-regression analyses of data from a 4-year population-based prospective study revealed that of the evaluated risk factors (male gender, child care attendance, smoke exposure, lack of breastfeeding, and other children in the house), only preterm birth and young chronologic age independently correlated with more severe RSV disease after adjusting for other covariates. In the professional opinion of specialized physicians reviewing the data, we have adopted this criterion.

3. **RSV, Prevention in a Patient with Hematopoietic Stem Cell Transplant (Bone Marrow Transplant [BMT], Peripheral Blood, Placental or Cord Blood) Who Does NOT Meet Any of the Approval Criteria Above.** Phase I studies in a total of 21 patients have evaluated Synagis in BMT patients. Guidelines (2009) co-sponsored by the Center for International Blood and Marrow Transplant Research (CIBMTR), National Marrow Donor Program (NMDP), European Blood and Marrow Transplant Group (EBMT), American Society for Blood and Marrow Transplant (ASBMT), Canadian Blood and Marrow Transplant Group (CBMTG), Infectious Diseases Society of America (IDSA), Society for Healthcare Epidemiology of America (SHEA), Association of Medical Microbiology and Infectious Diseases (AMMI), the CDC, and the Health Resources and Services Administration address RSV prevention in patients with hematopoietic stem cell transplant. These guidelines state preemptive aerosolized ribavirin is recommended by some for patients with RSV upper respiratory infection (URI), especially those with lymphopenia (during the first 3 months after hematopoietic stem cell transplant), and preexisting obstructive lung disease (late after hematopoietic stem cell transplant) the recommendation is based on retrospective studies as well as a prospective trial with inadequate accrual. Although a definitive, uniformly effective preemptive therapy for RSV infection among hematopoietic stem cell transplant recipients has not been identified, certain other strategies have been proposed, including systemic ribavirin, RSV antibodies (i.e., passive immunization with high RSV-titer intravenous immune globulin [IVIG], RSV immunoglobulin) in combination with aerosolized ribavirin, and RSV monoclonal antibody (mAb [e.g., Synagis]). No randomized trial has been completed to test the efficacy of these strategies; therefore, no specific recommendation regarding any of these strategies can be given at this time.

4. **RSV, Treatment of Disease.** There are limited data investigating Synagis for the treatment of established RSV infections. Passive antibody administration is not effective in treatment of RSV disease and is not approved or recommended for this indication. If any infant or young child receiving monthly Synagis prophylaxis experiences a breakthrough RSV hospitalization, monthly prophylaxis should be discontinued because of the extremely low likelihood of a second RSV hospitalization (< 0.5%).

5. **Wheezing, Prevention in a Patient Who Does Not Meet Any of the Approval Criteria.** Prophylaxis with Synagis is not recommended for primary asthma prevention or to reduce subsequent episodes of wheezing. In the professional opinion of specialized physicians reviewing the data, we have adopted this criterion.

Endorsed: September 17, 2014
Approved: October 14, 2014
Revised:
Reviewed:
REFERENCES

OTHER REFERENCES UTILIZED
2014-2015 Synagis® Seasonal Respiratory Syncytial Virus Enrollment Form

Synagis Prior Authorization Worksheet / Prescription Order Form

Please FAX this completed form and supporting documentation to:
1-419-887-2028 OR 1-866-214-2024

Synagis® (palivizumab)

SUPPORTING DOCUMENTATION IS REQUIRED FOR SYNAGIS REQUESTS (CHART NOTES, LAB RESULTS, ETC.)

PATIENT INFORMATION

<table>
<thead>
<tr>
<th>Member Number #</th>
<th>DOB</th>
<th>PRESCRIBER INFORMATION</th>
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MEDICAL INFORMATION

Diagnosis and Clinical Information (Please check ALL that apply)

- < 24 wks of gestation (765.21)
- 24 wks of gestation (765.22)
- 25-26 wks of gestation (765.23)
- 27-28 wks of gestation (765.24)
- 29-30 wks of gestation (765.25)
- 31-32 wks of gestation (765.26)
- 33-34 wks of gestation (765.27)
- Chronic Respiratory Disease arising in the perinatal period (CLD) (770.7)
- Congenital Heart Disease (Specify ICD-9): □
- Congenital Abnormality of Respiratory System (748.3-748.4)

Patient’s gestational age _____ wks ______ days
Current weight:________ g/kg/lbs / Date recorded: __________

Synagis Criteria is Based on the 2014 American Academy of Pediatrics Red Book Guidelines

MEDICAL AUTHORIZATION CLINICAL CRITERIA*

Prematurity
- ≤ GA 28 wks, 6 days AND < 12 months at start of RSV season

Chronic Lung Disease (CLD)
- Note: **CLD of prematurity defined as gestational age ≤ 31 weeks, 6 days, AND requirement for 21% oxygen for at least the first 28 days after birth.
- < 12 months of age at start of RSV season with CLD **
- 12-24 months of age with CLD ** AND continues to require medical support† during the 6-month period before second RSV season AND
  - Supplemental oxygen † for the 6 months prior to RSV season (dates/duration)
  - Diuretic therapy † (drugs/dates)
  - Chronic corticosteroids † (drugs/date)

Congenital Heart Disease (CHD)
- ≤ 12 months of age at start of season with hemodynamically significant CHD such as:
  - Acyanotic heart disease and receiving medication to control congestive heart failure and surgery to correct (drugs/dates) (surgery date)
  - Moderate to severe pulmonary hypertension
  - Other: describe

Airway / Neuromuscular Conditions
- < 12 months of age at start of RSV season and compromised handling of secretions AND due to:
  - Significant abnormality of the airway (attach clinical notes)
  - Neuromuscular condition (attach clinical notes)

Other medical history or condition
- Other medical history (describe)
- Bronchodilators (dates)

PRESCRIPTION INFORMATION

- Previous injections (including doses given in hospital) □ Yes □ No If yes, dates:
- Synagis® (palivizumab) 50mg and/or 100mg vials Date of first injection: __________
- Sig: Inject 15mg/kg IM one time per month _____ # doses (not vials) Delivery to: □ Patient’s home □ MD office
- Name of Home Health Agency:
- Specialty Pharmacy Name:

Prescriber’s Signature: __________________________ Prescriber’s NPI __________ Date: __________

*Pediatrics 2014;134;415; originally published online July 28, 2014 / http://pediatrics.aappublications.org/content/134/2/415.full.html