Medical Policy

BlueCross BlueShield of Kansas
An independent licensee of the Blue Cross Blue Shield Association

Title: Synagis (palivizumab)

- **Prime Therapeutics will review Prior Authorization**

  Prior Authorization Form:
  http://www.bcbsks.com/CustomerService/Forms/pdf/PriorAuth-1302KS-SYNA.pdf

  Link to Drug List (Formulary):
  http://www.bcbsks.com/CustomerService/PrescriptionDrugs/drug_list.shtml

Professional
Original Effective Date: December 20, 2002
Revision Date(s): October 31, 2002; February 1, 2003; February 1, 2004; November 1, 2005; July 1, 2006; November 2, 2006; March 22, 2007; June 1, 2007; December 7, 2009; December 9, 2011; October 26, 2012; October 16, 2013; October 9, 2014; November 4, 2014; September 1, 2015; October 1, 2016
Current Effective Date: October 1, 2016

Institutional
Original Effective Date: February 1, 2007
Revision Date(s): March 22, 2007; June 1, 2007; December 7, 2009; December 9, 2011; October 26, 2012; October 16, 2013; October 9, 2014; November 4, 2014; September 1, 2015; October 1, 2016
Current Effective Date: October 1, 2016

State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member's benefits, contact Blue Cross and Blue Shield of Kansas Customer Service.

The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.

The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.

DESCRIPTION

The intent of the Synagis (palivizumab) Prior Authorization (PA) program is to ensure that patients prescribed therapy meet the selection requirements defined in product labeling and/or clinical guidelines and/or clinical studies. The PA defines appropriate use as the Food and Drug Administration (FDA) labeled indication for the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) in pediatric patients at high risk of RSV infection as defined by American Association of Pediatrics (AAP) 2014 guidelines. Length of approvals will be recommended by the AAP guidelines.

Target Drug

Brand	Generic	Dosage Form
Synagis®	palivizumab	injection

FDA Approved Indications and Dosage[1]

FDA Indication*

For the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) in children at high risk of RSV disease. Safety and efficacy were established in children with bronchopulmonary dysplasia (BPD), infants with a history of premature birth (≤35 weeks gestational age), and children with hemodynamically significant congenital heart disease (CHD).

*The safety and efficacy of Synagis have not been established for the treatment of RSV disease.

Dosing*

The recommended dosage is 15 mg/kg via IM injection prior to commencement of the RSV season and remaining doses administered once monthly throughout the RSV season. Children undergoing cardiopulmonary bypass should receive an additional dose of Synagis as soon as possible after the cardiopulmonary bypass procedure (even if sooner than a month from the previous dose). Thereafter, doses should be administered monthly as scheduled.

POLICY

Prior Authorization (PA) Criteria for Approval

Synagis (palivizumab) will be approved for patients who have not exceeded the maximum recommended doses of palivizumab for the current respiratory syncytial virus (RSV) season when the following criteria are met:

1. The patient has not received the maximum recommended doses of Synagis (palivizumab) for the current respiratory syncytial virus (RSV) season
   AND

2. ONE of the following
   A. Patient's chronological age at the start of the RSV season is less than 12 months AND ONE of the following:
      1) Gestational age is <29 weeks 0 days
         OR
      2) The patient was a preterm infant who developed chronic lung disease of prematurity defined as gestational age (birth at) <32 weeks, 0 days, and a requirement for >21% oxygen for at least the first 28 days after birth
         OR
      3) The patient is profoundly immunocompromised during the RSV season (eg, severe combined immunodeficiency, solid organ/hematopoietic stem cell transplant, undergoing chemotherapy, or advanced acquired immunodeficiency)
         OR
      4) The patient has either congenital abnormalities of the airway or a neuromuscular condition that impairs the ability to clear respiratory tract secretions because of an ineffective cough
         OR
      5) The patient has cystic fibrosis (CF) AND clinical evidence of chronic lung disease (CLD) and/or nutritional compromise
         OR
      6) The patient has hemodynamically significant congenital heart disease and requires cardiac transplantation during the current RSV season
         OR
      7) The patient has hemodynamically significant congenital heart disease AND ONE of the following
         a) The patient is an infant with lesions adequately corrected by surgery but still requires medication for congenital heart disease (CHD) AND the following:
            i. The prescriber is a pediatric cardiologist or has consulted with a pediatric cardiologist
         b) The patient has cyanotic heart disease AND ALL of:
            i. The patient is receiving medication to control congestive heart failure

AND

ii. The prescriber is a pediatric cardiologist or has consulted with a pediatric cardiologist

OR

c) The patient has acyanotic heart disease and the patient is receiving medication to control congestive heart failure AND the patient will require a cardiac surgical procedure

OR

d) The patient has moderate to severe pulmonary hypertension

OR

B. Patient's chronological age at the start of the RSV season is 12 months to 24 months AND ONE of the following:
   1) The patient has hemodynamically significant congenital heart disease and requires cardiac transplantation during the current RSV season
      OR
   2) The patient has 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) AND continues to require medical support (chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) during the 6-month period before the start of the 2nd RSV season
      OR
   3) The patient is profoundly immunocompromised during the RSV season (eg, severe combined immunodeficiency, solid organ/hematopoietic stem cell transplant, undergoing chemotherapy, or advanced acquired immunodeficiency)
      OR
   4) The patient has cystic fibrosis (CF) AND manifestations of severe lung disease (previous hospitalization for pulmonary exacerbation in the 1st year of life or abnormalities on chest radiography or chest computed tomography that persist when stable) or has weight for length less than the 10th percentile

Length of approval:

Up to 5 doses until March 31 EXCEPT the following:

- Patients who have hemodynamically significant congenital heart disease and who will undergo a surgical procedure involving cardiopulmonary bypass or extra-corporeal membrane oxygenation during the RSV season and who will continue to require prophylaxis after the surgical procedure may receive one extra dose of Synagis (palivizumab) after bypass or at the conclusion of the extra-corporeal membrane oxygenation (up to 6 doses per RSV season).

RATIONALE

Palivizumab is the only product labeled for prevention of RSV lower respiratory tract disease and is approved for use in children with chronic lung disease (CLD), children with a history of preterm birth (equal to or less than 35 weeks gestation), or children with hemodynamically significant congenital heart disease (CHD).[2] Use of palivizumab has demonstrated efficacy in preventing RSV hospitalization rates in high risk infants.[3] Data from the Impact-RSV trial indicates a fifty-five percent reduction in RSV hospitalization rates in high risk infants receiving palivizumab compared to placebo (4.8 percent versus 10.6 percent, $p < 0.001$).[3] A study of infants and children with hemodynamically significant congenital heart disease demonstrated a 45% decrease in the rate of hospitalization due to RSV (9.7% and 5.3% in placebo versus palivizumab, respectively [p=0.003]). Among different groups of high-risk infants, hospitalization rates attributable to RSV were reduced by 39% to 82%, relative to control groups.[2,4]

The RSV season in the Northern hemisphere is typically November 1 to March 1, although communities in the southern United States, particularly in Florida, may experience earlier onset of RSV (July).[2] The severity of the season, the time of onset, the peak of activity, and the end of the season cannot be predicted precisely and there may be substantial variation in timing of community outbreaks from year to year in the same community and between communities in the same region.[2] These overall variations, however, occur within the overall pattern of RSV outbreaks, usually beginning in November or December, peaking in January or February, and ending by March.[2] Despite various dates of onset, children who qualify for prophylaxis for the entire RSV season, should be administered palivizumab only during the five months following the onset of RSV season in their region (maximum of five doses).[2] Infants and children with CLD, CHD, or birth before 32 weeks, 0 days gestation who initiate treatment after the start of the RSV season will not require all five doses.[2]

The 2014 AAP recommendations for palivizumab use consider the following infants and children as appropriate recipients of therapy:[2]

1. Infants born before 29 weeks, 0 days gestation or earlier and are less than 12 months of age at the start of RSV season. These patients should receive a maximum of five doses.

2. Infants born at 29 weeks 0 days gestation or later may quality to receive prophylaxis on the basis of congenital heard disease (CHD), chronic lung disease (CLD), or another condition.

3. Infants less than 12 months old who were preterm infants who develop chronic lung disease of prematurity defined as gestational age (birth at) <32 weeks, 0 days and a requirement for >21% oxygen for at least the first 28 days after birth. During the 2nd year (12-24 months) of life who develop 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 AND continue to require medical support (chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) during the 6-month period before the start of the 2nd RSV season.

4. Infants less than 12 months with hemodynamically significant CHD who are most likely to benefit from immunoprophylaxis include infants with acyanotic heart disease who are receiving medication to control congestive heart failure (CHF) and will require cardiac surgical procedures and infants with moderate to severe pulmonary hypertension.

a. Infants less than 12 months with cyanotic heart defects should consult with a pediatric cardiologist for a prophylaxis decision.
b. Infants/children with CHD that should NOT receive immunoprophylaxis are:
    1) Those with hemodynamically insignificant heart disease (eg, 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 medication for CHD is required
    3) Infants with mild cardiomyopathy who are not receiving medical therapy
    4) Children in 2nd year of life.

5. Children younger than 24 months with hemodynamically significant CHD who are currently receiving prophylaxis and who continue to require it after a surgical procedure, a post-operative dose should be considered after cardiac bypass or at the conclusion of extra-corporeal membrane oxygenation.

6. Children younger than 24 months with hemodynamically significant CHD who are undergoing cardiac transplantation during the RSV season.

7. Infants younger than 12 months with neuromuscular disease or congenital anomaly that impairs the ability to clear secretions from the upper airway because of ineffective cough.

8. May be considered in:
    a. Children younger than 24 months who are profoundly immunocompromised during the RSV season.
    b. Infants younger than 12 months with cystic fibrosis with clinical evidence of CLD and/or nutritional compromise
        1) Continuation into the 2nd year for infants with manifestations of severe lung disease (previous hospitalization for pulmonary exacerbation in the 1st 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.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT/HCPCS

90378 Respiratory syncytial virus, monoclonal antibody recombinant, for intramuscular use, 50 mg, each

REVISIONS

03-22-2007 effective	In “Policy” section 2, b., changed the word ‘through’ to ‘to’ and added ‘(i.e. 32 weeks, 0 days)’.

06-01-2007	In "Policy" section 2, c., changed '33' to '32' and added '(i.e. between 32 weeks, 1 day and 35 weeks, 0 days)'.
12-07-2009	In Header: ▪ Title changed to include "Synagis" ▪ Added links to information concerning Prior Authorization information and Prior Authorization forms.
	In Description section: ▪ Updated description.
	In Policy section: ▪ Updated policy with American Academy of Pediatric (AAP) 2009 updated criteria for use of Palivizumab for prevention of respiratory syncytial virus infections From: "RSV-Ig is medically necessary and administered once a month during the RSV season (November through April) when the following apply: 1. CLD (Bronchopulmonary dysplasia) • Children less than two (2) years of age with CLD that have required medical treatment, i.e., oxygen, steroids, bronchodilators, for their CLD within the last six months. 2. Prematurity a. Infants born at 28 weeks of gestation or less may receive prophylaxis if less than or equal to 12 months (<12 months) of age at the start of RSV season. b. Infants born at 29 to 32 weeks of gestation (i.e. 32 weeks, 0 days) may receive prophylaxis if less than or equal to 6 months (<6 months) of age at the start of RSV season. c. Infants born at 32 to 35 weeks gestation (i.e. between 32 weeks, 1 day and 35 weeks, 0 days) 1) With CLD on medications or treatment (e.g. supplemental oxygen, bronchodilator, diuretic or corticosteroid therapy) within the past six months or 2) Prophylaxis of infants without CLD should be reserved for only those infants who are at the greatest risk of severe infection as defined by two or more of the following risk factors: child care attendance, school-aged siblings, exposure to environmental air pollutants (excluding caregiver smoking), congenital abnormalities of the airways, or severe neuromuscular disease (causing significant respiratory impairment) and less than or equal to six months (<6 months) of age at the start of the RSV season. 3. Heart Disease a. Because of the decrease in palivizumab (Synagis®) after the use of cardiopulmonary bypass, a post-operative dose of palivizumab (Synagis®) should be considered. b. Prophylaxis for infants younger than 24 months of age with congenital heart disease is considered medically necessary for an infant (must meet only one of the following): 1) Receiving medication to control congestive heart failure, or 2) With moderate to severe pulmonary hypertension, or 3) With cyanotic heart disease. 4. Although specific recommendations for all immunocompromised patients cannot be made, children with severe immunodeficiencies may benefit from RSV-Ig. Providers may consider substituting RSV-Ig during the RSV season for patients receiving IGIV monthly. 5. Treatment for RSV may be administered in the physician's office, outpatient setting, outpatient hospital setting, or a home health visit. Not Medically Necessary 1. Prophylaxis is not considered medically necessary for: a. An infant 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), b. An infant with lesions adequately corrected by surgery unless they continue to require medication for congestive heart failure, or c. An infant with mild cardiomyopathy who is not receiving medical therapy. d. Children greater than two years of age." To the current policy language.
	In Rationale section: ▪ Rationale section added.
	Coding section deleted.
12-09-2011	Formatting changes to the Policy section.
	Updated Rationale.
	Updated References.
10-26-2012	In the Policy section: • In Item #5, moved "(supplemental oxygen, bronchodilator, diuretic, or chronic corticosteroid therapy)" after "medical therapy" to read "Chronological age is less than 24 months at the start of RSV season and the patient has required medical therapy (supplemental oxygen, bronchodilator, diuretic, or chronic corticosteroid therapy)..."
10-16-2013	In Policy Title, removed "(Respiratory Syncytial Virus [RSV]) Prior Authorization Criteria" to read "Synagis ".
	Updated Links to Prior Authorization
	Updated Rationale section.
	Added Coding section.
	Updated Reference section.
10-09-2014	Description section updated
	In Policy section: ▪ Updated policy with American Academy of Pediatric (AAP) 2014 Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection From: "Synagis will be approved for patients who have not exceeded the maximum recommended doses of palivizumab for the current respiratory syncytial virus (RSV) season (five doses per season EXCEPT for patients born between 32 weeks, 0 days and 34 weeks, 6 days gestation whose age at the beginning of RSV season is less than 3 months. These patients are limited to 3 doses per season.) if ONE of the following is met: 1. Gestational age is 28 weeks (28 weeks 6 days) or less and chronological age at the beginning of RSV season is twelve months or less OR 2. Gestational age is greater than 29 weeks (29 weeks, 0 days) but less than 32 weeks (31 weeks, 6 days) and chronological age at the beginning of RSV season will be less than or equal to six months OR 3. Gestational age is 32 weeks or greater (32 weeks, 0 days) but less than 35 weeks (34 weeks, 6 days) and chronological age at the beginning of RSV season is less than 90 days and the patient has at least one of the following two risk factors; 1) child care attendance (defined as a home or facility where care is provided for any number of infants or young toddlers in the child care facility), or 2) one or more siblings or other children younger than 5 years of age live permanently in the same household OR 4. Chronological age is less than 24 months at the start of RSV season and the patient is diagnosed with congenital heart disease, with one of the following factors; requires cardiopulmonary bypass during the current RSV season (one additional dose is allowed if patient has surgery requiring cardiopulmonary bypass during prophylaxis therapy), patient is receiving medication to control congestive heart failure, patient has cyanotic heart disease, or patient has moderate to severe pulmonary hypertension OR 5. Chronological age is less than 24 months at the start of RSV season and the patient

	has required medical therapy (supplemental oxygen, bronchodilator, diuretic, or chronic corticosteroid therapy) for chronic lung disease within the six months prior to the beginning of RSV season OR 6. Chronological age is less than 24 months at the start of RSV season and the patient has been diagnosed with severe immunodeficiency (e.g., severe combined immunodeficiency or advanced acquired immunodeficiency) OR 7. Chronologic age is less than 12 months at the start of RSV season and patient has either congenital abnormalities of the airway or a neuromuscular condition that compromises handling of respiratory tract secretions Length of approval: Approvals will be for up to 5 doses until March 31 EXCEPT: • Patients whose gestational age at the start of RSV season is 32 weeks or greater (32 weeks, 0 days) but less than 35 weeks (34 weeks, 6 days) and chronological age at the beginning of RSV season is less than 90 days (approval for up to 3 doses until age 90 days) • Patients with CHD requiring surgery involving cardiopulmonary bypass during RSV prophylaxis therapy (approval for one extra dose)" To the current policy language.
	Rationale section updated
	In Coding section: ▪ CPT coding confirmed
	References updated
11-04-2014	In Policy section: ▪ In Item #2, A., 7), added, "a) The patient has cyanotic heart disease AND ALL of: i. The patient is receiving medication to control congestive heart failure, AND ii. The prescriber is a pediatric cardiologist or has consulted with a pediatric cardiologist."
	In Rationale section: ▪ Removed the "Table 1. Maximum Number of Synagis (palivisumab) Doses for RSV Prophylaxis of Preterm Infants Without Chronic Lung Disease (CLD), Based on Birth Date and Gestational Age (Shown for Areas Beginning Prophylaxis on November 1st)" table.
09-01-2015	Updated Description section.
10-01-2016	In Policy section: ▪ Added new Item 2 A 7 a, "The patient is an infant with lesions adequately corrected by surgery but still requires medication for congenital heart disease (CHD) AND the following: i. The prescriber is a pediatric cardiologist or has consulted with a pediatric cardiologist". ▪ Re-lettered remaining items in Item 2 A 7.
	Updated References section.

REFERENCES

1. Synagis prescribing information. Medimmune, Inc. March 2014.
2. The American Academy of Pediatrics Committee on Infectious Diseases. Policy Statement: Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection. Committee on Infectious Diseases And Bronchiolitis Guidelines Committee. *Pediatrics.* DOI: 10.1542/peds.2014-1665. http://pediatrics.aappublications.org/content/134/2/415. Accessed August 6, 2014.

3. 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;102:531-537.
4. Feltes TF, Cabalka AK, Meissner HC, et a*l. Paliviz*umab prophylaxis reduces hospitalization due to respiratory syncytial virus in young children with hemodynamically significant congenital heart disease. *J Pediatr* 2003;143:532-540.

Other References

1. Blue Cross and Blue Shield of Kansas Family Practice Liaison Committee, July 11, 2006 (see Blue Cross and Blue Shield of Kansas Newsletter, Blue Shield Report. MAC–03-06).
2. Blue Cross and Blue Shield of Kansas Liaison Pediatric Committee, August 2, 2006 (see Blue Cross and Blue Shield of Kansas Newsletter, Blue Shield Report. MAC–03-06).
3. Blue Cross and Blue Shield of Kansas Medical Advisory Committee (MAC) meeting, November 2, 2006 (see Blue Cross and Blue Shield of Kansas Newsletter, Blue Shield Report. MAC–03-06).
4. Blue Cross and Blue Shield of Kansas Medical Consultant, Practicing Board Certified Pediatrician (202), December 2005.
5. Blue Cross and Blue Shield of Kansas Family Practice Liaison Committee, July 2007, July 2009, July 2010.
6. Blue Cross and Blue Shield of Kansas Pediatric Liaison Committee, August 2007, August 2008, July 2009, July 2011; July 2015.
7. Blue Cross and Blue Shield of Kansas Medical Consultant, Practicing Board Certified Pediatrician (535), January 2009.
8. Blue Cross and Blue Shield of Kansas Family Practice Liaison Committee CB, November 2009.