Effective for dates of service on or after September 1, 2014, refer to: https://www.bcbsal.org/providers/pharmPolicies/draft/0312.pdf

Name of Policy:
Immune Prophylaxis for Respiratory Syncytial Virus: Synagis® (Palivizumab)

Policy #: 302
Category: Pharmacology
Latest Review Date: August 2013
Policy Grade: B

Background/Definitions:
As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:
1. The technology must have final approval from the appropriate government regulatory bodies;
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;
3. The technology must improve the net health outcome;
4. The technology must be as beneficial as any established alternatives;
5. The improvement must be attainable outside the investigational setting.

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. In accordance with generally accepted standards of medical practice; and
2. Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient’s illness, injury or disease; and
3. Not primarily for the convenience of the patient, physician or other health care provider; and
4. Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient’s illness, injury or disease.
Description of Procedure or Service:
Respiratory Syncytial Virus (RSV) is the most common cause of lower respiratory tract infections in infants and young children. Almost all children have been infected with RSV by age two years. Children at highest risk include those who are less than two years old with prematurity, chronic lung disease (CLD, [formerly known as bronchopulmonary dysplasia]), congenital heart disease (CHD), multiple congenital anomalies, and certain immunodeficiencies. Immune prophylaxis against RSV is a prevention strategy to reduce the incidence of infection and its associated morbidity, including hospitalization, in high-risk infants.

Respiratory syncytial virus infections typically occur in the winter months, starting from late October to mid-January and ending from March to May. According to the 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 two-week period. During 1997-2006, an estimated 132,000-172,000 children aged < five years were hospitalized for RSV infection annually in the United States.

Chronic lung disease (CLD, [formerly known as bronchopulmonary dysplasia]) 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.

In contrast to the well-documented beneficial effect of breastfeeding against many viral illnesses, existing data are conflicting regarding the specific protective effect of breastfeeding against RSV infection. Breastfeeding should be encouraged for all infants in accordance with recommendations of the American Academy of Pediatrics (AAP). High-risk infants should be kept away from crowds and from situations in which exposure to infected people cannot be controlled. Participation in group child care should be restricted during the RSV season for high-risk infants whenever feasible. Parents should be instructed on the importance of careful hand hygiene. In addition, all high-risk infants six months of age and older and their contacts should receive influenza vaccine, as well as other recommended age-appropriate immunizations.

Currently, there is no vaccine available for RSV. However, prophylaxis with palivizumab (Synagis®) has been shown to reduce the risk of hospitalization in high-risk infants and young children. Synagis® is a humanized RSV monoclonal antibody and is administered by intramuscular injection in monthly doses of 15 mg/kg of body weight. It is administered once a month during the RSV season, usually a total of 3-5 doses, with the first dose in October or November and the last dose at the beginning of March.
Policy:

**Effective for dates of service on or after September 1, 2014, refer to:**

**Effective for dates of service on or after September 24, 2009 and prior to September 1, 2014:**

*Synagis*® (palivizumab), for the prevention of serious lower respiratory tract disease caused by the respiratory syncytial virus (RSV) in pediatric patients at high-risk of RSV disease, *meets* Blue Cross and Blue Shield of Alabama’s medical criteria for coverage when the following criteria are met:

1. Infants and children < 24 months of age at initiation of therapy with chronic lung disease of prematurity (CLD, [formerly known as Broncho Pulmonary Dysplasia]) who required medical therapy for CLD within six months of the RSV season.
2. Infants born ≤ 28 weeks’ gestation and are ≤ 12 months chronological age at the start of the RSV season.
3. Infants born at 29-32 weeks’ gestation and are ≤ 6 months chronological age at the start of the RSV season.
4. Infants born at 32 to < 35 weeks’ gestation and are ≤ 3 months chronological age at the start of the RSV season and have at least one risk factor, such as child care attendance or a sibling < age 5 years. These infants should receive a maximum of three monthly doses, up until they reach age 3 months.
5. Children with cystic fibrosis with pulmonary complications.
6. Infants with congenital abnormalities of the airway or neuromuscular disease.
7. Infants and children ≤ 24 months of age with hemodynamically significant congenital heart disease.
8. Infants and children with severe immunodeficiencies, such as severe combined immunodeficiency or advanced acquired immunodeficiency syndrome.

Once an infant or child qualifies for initiation of prophylaxis at the start of the RSV season, administration should continue throughout the season until the patient receives a maximum of five monthly doses, except as noted above in #4.

**Effective for dates of service prior to September 24, 2009:**

*Synagis*® (palivizumab), for the prevention of serious lower respiratory tract disease caused by the respiratory syncytial virus (RSV) in pediatric patients at high-risk of RSV disease, *meets* Blue Cross and Blue Shield of Alabama’s medical criteria for coverage when the following criteria are met:

1. Infants and children ≤ 24 months of age at initiation of therapy with chronic lung disease (CLD) who required medical therapy for CLD within 6 months of the RSV season.
2. Pre-term infants born ≤ 28 weeks of gestation and are ≤ 12 months chronological age at the start of the RSV season.
3. Pre-term infants born at 29-32 weeks of gestation and are ≤ 6 months chronological age at the start of the RSV season.
4. Pre-term infants born at 33-35 weeks of gestation and are ≤ 6 months chronological age at the start of the RSV season, with additional risk factors identified, such as childcare attendance, school-aged siblings, exposure to environmental air pollutants, congenital abnormalities of the airway, or severe neuromuscular disease.

5. Children with cystic fibrosis with pulmonary complications.

6. Children < 2 years of age who have congenital heart disease.

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the members' contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

**Key Points:**

There are several randomized clinical trials that have demonstrated the success of immune prophylaxis of respiratory syncytial virus (RSV).

In 1997, the PREVENT Study Group reported on a trial that randomized 510 infants with prematurity or bronchopulmonary dysplasia (BPD) to receive either placebo or RSV-IVIg infusions monthly for five months. The authors reported a 41% reduction in hospitalization due to RSV infection, and reductions in other measures of severity when it did occur.

In 1998, the Impact Study Group reported similar results with Palivizumab. They reported on a trial that randomized 1502 children with prematurity or BPD to receive five injections of either palivizumab or placebo. The results showed there was a 55% reduction in hospitalization and similar reductions in other measures of RSV severity in breakthrough infections. Palivizumab was safe and well tolerated.

In 1998, the American Academy of Pediatrics (AAP) published revised guidelines regarding the use of RSV-IVIg or palivizumab for RSV immune prophylaxis, which focused on infants with chronic lung disease and preterm infants.

In 2003, the AAP Red Book, which summarizes immunization recommendations, and the AAP Policy Statement on the prevention of RSV, added indications for children with hemodynamically significant heart disease. These guidelines form the basis of this policy and are summarized in the policy statement.

The AAP gave more restrictive recommendations for infants born between 32 weeks gestation and up to 35 weeks gestation, and the AAP Red Book adds the following: “Although palivizumab and RSV-IVIg have been shown to decrease the likelihood of hospitalizations in infants born between 32 and 35 weeks gestation, the cost of administering prophylaxis to this large group of infants must be considered carefully. Therefore, most experts recommend that prophylaxis should be reserved for infants in this group who are at greatest risk of severe
infection and who are younger than six months of age at the start of the RSV season. Epidemiologic data suggest that RSV infection is more likely to lead to hospitalization for these infants when the following risk factors are present: child care attendance, school-aged siblings, exposure to environmental air pollutants, congenital abnormalities of the airways or severe neuromuscular disease. However, no single risk factor causes a very large increase in the rate of hospitalization, and the risk is additive as the number of risk factors for an individual infant increases. Therefore, prophylaxis should be considered for infants between 32-35 weeks gestation only if two or more of these risk factors are present”.

Immune prophylaxis has also been suggested for patients 24 months of age or younger with congenital heart disease (CHD). The AAP guidelines note that children with cyanotic CHD who received RSV-IVIg and underwent cardiac surgery appeared to experience an increased surgical mortality rate. Therefore, according to the AAP guidelines, RSF-IVIg is contraindicated in children with cyanotic CHD. FDA labeling for Synagis was revised in September 2003 to include children and infants with hemodynamically significant congenital heart disease. This is based on a study published by Feltes, et al (2003). This was a double-blind, placebo-controlled trial of 1287 children with hemodynamically significant CHD who were randomized to receive palivizumab or placebo. The results showed a total of 9.7% of the placebo group required hospitalization, compared to 5.3% of the treatment group. The results showed that palivizumab significantly reduced the rate of hospitalizations, hospital days, and days of increased oxygen usage in children with serious CHD. The proportions of subjects who experienced adverse events were similar in both groups.

The 2003 AAP guidelines indicate the use of palivizumab in children with CHD should be based on the degree of physiological cardiovascular impairment. Infants most likely to benefit from immunoprophylaxis include those receiving medication to control congestive heart failure, those with moderate to severe pulmonary artery hypertension, and infants with cyanotic heart disease. These guidelines also concluded that the following groups of infants are not at increased risk of RSV generally should not receive immunoprophylaxis: infants and children with hemodynamically insignificant heart disease (e.g., secundum atrial septal defects, small VSDs, pulmonic stenosis, uncomplicated aortic stenosis, mild coarctation of the aorta, and PDA). In addition, prophylaxis is not necessary in infants with lesions adequately corrected by surgery unless they continue to require medicine for CHF, and infants with cardiomyopathy who are not receiving medical therapy.

The use of RSV-IVIg or palivizumab in patients with documented immunodeficiencies has also been suggested. The AAP guidelines note: “Palivizumab or RSV-IVIg has not been evaluated in randomized trials in immunocompromised children. Although specific recommendations for immunocompromised patients cannot be made, children with severe immunodeficiencies (e.g., severe combined immunodeficiency or severe acquired immunodeficiency syndrome) may benefit from prophylaxis.”

Immunocompromised patients undergoing stem-cell transplantation are also at risk for potentially lethal viral respiratory infections. Cortez, et al (2002), reported on 32 patients undergoing allogenic hematopoietic stem-cell transplantation were given RSV immune globulin (RSVIG) at the time of transplantation and three weeks later. Antibody titers to RSV and other
respiratory viruses were measured at baseline and over the subsequent six weeks. Baseline antiviral titers and increases in antibody after administration of RSVIG were extremely variable for all viruses.

On October 1, 2003, MedImmune and Massachusetts Public Health and Biologics Laboratory (MPHBL), the manufacturers of RespiGam Respiratory Syncytial Virus Immune Globulin (RSV-IVIg), announced that the production of this product will be discontinued. As of March 15, 2004, all current inventory levels of RespiGam had been depleted and no product is available for sale from MedImmune or MPHBL.

The AAP guidelines currently recommend five monthly doses of palivizumab given during the RSV season, which typically occurs from November to April. Within the United States, the inevitability of the RSV season is predictable, but the severity of the season and time of onset are variable from year to year and also between geographic areas within a given year. This has led to discussions on either earlier or later immunoprophylaxis, or greater than five monthly doses. Nevertheless, as pointed out by Meissner and colleagues from the Centers for Disease Control and Prevention, “…this yearly and regional variation still occurs within the overall pattern of RSV outbreaks, usually beginning in November or December, peaking in January or February, and ending by March. Communities in the southern region tend to experience the earliest onset of RSV activity, and midwestern states tend to experience the latest onset, but community to community variation in timing precludes using either national or regional data to precisely predict individual community RSV outbreaks. The duration of the season for western and northeast regions typically occurs between that noted in the South and Midwest.” The authors point out that the recommendation for 5 monthly doses is derived from the randomized studies of palivizumab. A serum palivizumab concentration of ≥ 30 µg/mL is the target level for protection, and in randomized studies, the trough level of palivizumab exceeded 30 µg /mL for at least 30 days after the fifth dose. This indicates that five monthly doses will provide substantially more than 20 weeks of protective serum antibody levels, covering most of the RSV season even with variation in season onset and end. The state health department or a diagnostic virology laboratory may be helpful to determine the optimal time to begin administration.

Typically, a total of five monthly doses are given during the RSV winter season. Once a child qualifies for initiation of prophylaxis at the start of the RSV season, administration should continue throughout the season and not stop even if the infant reaches 6-12 months of age. Administration of RSV prophylaxis beyond the RSV season is considered medically necessary only if the Centers for Disease Control and Prevention (CDC) or a local health department reporting to and confirmed by the CDC, indicates an outbreak of RSV in the patient’s geographic area that persists beyond the RSV season.

Information concerning an RSV outbreak in a certain geographic area may be obtained from CDC surveillance summaries of weekly RSV laboratory test result data posted at http://www.cdc.gov/surveillance/nrevss/rsv-reg-trends.htm

Also, surveillance summaries for RSV are published periodically in the Morbidity and Mortality Weekly and reports may be obtained from http://www.cdc.gov/mmwr/.
**2009 Update**
The policy was updated based on the revised guidelines issued by the American Academy of Pediatrics.

**October 2010 Update**
Two systematic reviews were identified: one reviewing compliance with palivizumab and one reviewing the use in children with cystic fibrosis.

A Cochrane review was published in 2010 and updated in 2012, assessing the use of palivizumab in children with cystic fibrosis (CF). One randomized comparative trial met the inclusion criteria of both reviews. In the study, 186 infants under the age of two with CF were randomized to receive five monthly doses of palivizumab (n=92) or placebo (n= 94). One member of each group was hospitalized for RSV within the six-month follow-up period. The rate of adverse event noted in each group was relatively high, with serious adverse events not significantly different between the palivizumab and placebo groups (20.2% and 17.3%, respectively). The authors noted that it was not possible to draw conclusions on the tolerability and safety of RSV immune prophylaxis in CF. The single study reported similar adverse events, but not specify how adverse events were classified. No clinically meaningful outcome differences were noted at six-month follow-up. The authors of the review called for additional randomized studies to establish both efficacy of immune prophylaxis in children with CF.

Frogel et al (2010) reviewed the medical literature on compliance with palivizumab therapy, and the relation between hospitalization rates in fully compliant and less compliant groups. A total of 25 articles and abstracts met review inclusion criteria. Significant heterogeneity was detected due to between-study differences in the populations studied, and the definition of compliance used. Differences in compliance definitions led to a compliance rate range of 25% to as high as 100%, compared to rates in licensing studies of 92% and 93%. This led the authors to be conclusion that compliance in practice is far more variable. Minorities and patients on Medicaid were less likely to receive the full complement of palivizumab doses, while patients participating in a home health program tended to have higher compliance and less hospitalization. Home health programs were defined as nurse delivered injections performed in the home setting.

At this time the policy statements remain unchanged.

**2012 Update**
In August 2009, AAP released a policy statement (including references and evidence grading) that supported their revised indications for the use of palivizumab for the prevention of respiratory syncytial virus infections. In commenting on their 2009 recommendations, the AAP policy statement indicates, "they [the 2009 AAP recommendations] specifically target infants in this [32 to less than 35 weeks' gestational age] with consistently identified risk factors for RSV hospitalization during the period of greatest risk, which is the first three months of life.”

In 2008, Cohen and colleagues evaluated the characteristics of patients (n=19,548) enrolled in The Palivizumab Outcomes Registry with CHD over the four RSV seasons. The Palivizumab Outcomes Registry prospectively collected data on patients who received RSV prophylaxis with palivizumab during the 2000–2004 RSV seasons. The percentage of registry subjects with CHD
increased from 4.8% (102/2,116) in the first season to 11.4% (688/6,050) in the last season. Across all four seasons, 1,500 subjects with CHD were enrolled; 71% of whom had acyanotic CHD. The proportion with cyanotic CHD increased from 19.6% (20/102) in the 2000–2001 season to 37.5% (258/688) in the 2003–2004 season, while the proportion of all CHD in the registry more than doubled during this time. The cumulative RSV hospitalization rate was 1.9% among patients with CHD who received prophylaxis. Among subjects with cyanotic and acyanotic CHD, hospitalization rates were 2.6% and 1.6%, respectively. The authors concluded, “…the prospective data collected in the Palivizumab Outcomes Registry provides the largest published dataset available on infants with CHD receiving palivizumab; shows low hospitalization rates, use consistent with pre-licensure clinical trial data and the revised American Academy of Pediatrics guidelines.”

A review article discussed the development of a second-generation humanized monoclonal antibody (mAb), motavizumab, which is no longer under study in Phase III clinical trials, and most recently, a third generation mAb, Numax-YTE.

In a literature review, Hynicka and Ensor found data are limited on RSV prophylaxis in immunocompromised adult patients. The only prospective study identified in the review was by Kassis et al. in which intravenous palivizumab was given to 16 high-risk stem-cell transplant patients to prevent the nosocomial spread of RSV infection from five stem-cell transplant patients. After one week, no further RSV cases occurred, but whether controlling the spread of RSV on the stem-cell transplant unit was related to RSV prophylaxis versus implementation of strict quarantine and infection control practices cannot be determined.

2013 Update
High-risk Infants
Systematic Reviews
In 2008, the Department of Public Health and Epidemiology, University of Birmingham, Birmingham, UK, released a Health Technology Assessment (HTA) on immunoprophylaxis against respiratory syncytial virus (RSV) with palivizumab in children. This HTA report was updated in 2011; the update developed the economic model from the first report by cost-effectiveness in different subgroups of children with RSV infection. Thirteen studies published through August 2009 were included in this updated analysis. Most of the studies were small and not powered for the outcomes of interest, and the quality of reporting was also frequently poor. In the original HTA report, two randomized controlled trials (RCTs) (summarized below) were used for establishing the relative risk of hospitalization in children given palivizumab compared with those without. No additional RCTs of palivizumab were found for the HTA update in 2011.

Randomized Controlled Trials
Several RCTs have demonstrated the success of immune prophylaxis of (RSV). In 2013, Blanken and colleagues performed a multicenter, double-blind, randomized, placebo-controlled MAKI trial to investigate the potential causal role of RSV infection in the pathogenesis of wheezing illness during the first year of life, using palivizumab. The trial randomly assigned 429 otherwise healthy preterm infants born at a gestational age of 33 to 35 weeks to receive either monthly palivizumab injections (214 infants) or placebo (215 infants) during the RSV
season. The pre-specified primary outcome was the total number of parent-reported wheezing days in the first year of life. Premature infants treated with palivizumab had a significant 61% relative decrease in the total number of wheezing days during the first year of life (95% confidence interval [CI]: 56 to 65). Moreover, the effect of RSV prevention on the number of wheezing days persisted in the post-prophylaxis period (i.e., starting at two months after the last injection) for a relative reduction of 73% (95% CI: 66 to 80). In addition, palivizumab treatment reduced hospitalizations related to RSV infection (12.6% in the RSV prevention group, as compared with 21.9% in the placebo group (p=0.04).

The 2003 recommendation by the AAP was based on the results of the Feltes RCT noted above. In 2009, AAP updated its guidelines regarding the use of immune prophylaxis for respiratory syncytial virus (RSV). The new AAP Red Book 2012 chapter on RSV was reviewed and no substantive changes noted. The following is a summary, provided by the AAP, of the major changes that were made to the 2009 guidelines:

1. Recommendations for initiation and termination of prophylaxis are modified to reflect current CDC descriptions of RSV seasonality in different geographic locations within the United States.

2. The recommendations remain unchanged for infants with congenital heart disease, chronic lung disease of prematurity and birth before 32 weeks' gestation.

3. Regardless of the month when the first dose is administered, the recommendation for a maximum number of five doses for all geographic areas is emphasized for infants with hemodynamically significant congenital heart disease, chronic lung disease of prematurity or birth before 32 weeks' gestation and for a maximum number of three doses for infants with a gestational age of 32 to 35 weeks without hemodynamically significant congenital heart disease or chronic lung disease.

4. Risk factors for severe RSV lower respiratory tract disease among infants born between 32 to 35 weeks' gestation have been modified to include only:
   a. Infant attends child care
   b. Siblings living in the household are less than five years of age

5. Infants 32 to 35 weeks' gestation age who are born within the three months before the onset of RSV season and throughout the RSV season will qualify for prophylaxis if they have at least one [of the modified] risk factors. Earlier recommendations required two of five [different] risk factors.

6. Infants who qualify for prophylaxis in the 32 to 35 weeks' gestation age group should receive prophylaxis only until they reach 90 days of age or a maximum of three doses (whichever comes first). This is a change from the previous recommendation for five months of prophylaxis.

7. The AAP's definition of gestational age is used throughout this document. For example, 32 to 35 weeks' gestation is defined as 32 weeks, 0 days through 34 weeks, 6 days.”
In August 2009, AAP released a policy statement (including references and evidence grading) that supported their revised indications for the use of palivizumab for the prevention of respiratory syncytial virus infections. In commenting on their 2009 recommendations, the AAP policy statement indicates, "they [the 2009 AAP recommendations] specifically target infants in this [32 to less than 35 weeks' gestational age] with consistently identified risk factors for RSV hospitalization during the period of greatest risk, which is the first three months of life.”

Clinical Input Received through Physician Specialty Societies and Academic Medical Centers
In response to requests, input was received through three physician specialty societies (seven responders) while this policy was under review in 2009. While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted. Almost all of those providing input agreed with the policy statements approved in October 2009; these statements are in agreement with the 2009 AAP guidelines.

Summary
Respiratory syncytial virus (RSV) is the most common cause of lower respiratory infections in children. At highest risk are those younger than two years of age with prematurity, chronic lung disease (CLD, [formerly known as bronchopulmonary dysplasia]), congenital heart disease, or multiple congenital anomalies. Immune prophylaxis against RSV is a prevention strategy to reduce the incidence of infection and its associated morbidity, including hospitalization, in high-risk infants.

Based on the weight of the clinical evidence from randomized clinical trials, systematic reviews and strong clinical consensus, immune prophylaxis for RSV has demonstrated reductions in RSV-related hospitalizations in select populations of susceptible infants and children. Therefore, immune prophylaxis for RSV may be considered medically necessary for the patients listed in the policy statement above. For all other uses of immune prophylaxis, the clinical evidence is not convincing that RSV hospitalizations will decrease. Therefore, the policy statements above note indications which are considered investigational or not medically necessary. The policy statements are in agreement with the 2009 American Academy of Pediatrics Guidelines.

Practice Guidelines and Position Statements
In 2003, the AAP released a policy statement with revised indications for the use of palivizumab and RSV-IVIg for the prevention of RSV infections.

In June 2009, the AAP released updated guidelines regarding the use of immune prophylaxis for RSV. The updated guidelines were published in the new AAP Red Book 2009 in the chapter on RSV.
In August 2009, the AAP released a policy statement (including references and evidence grading) with revised indications for the use of palivizumab for the prevention of RSV infections.

**Key Words:**
Synagis, palivizumab, RespiGam, RSV-IVIg, respiratory syncytial virus (RSV), chronic lung disease (CLD), bronchopulmonary dysplasia (BPD), congenital heart disease (CHD), immunoprophylaxis

**Approved by Governing Bodies:**
On June 19, 1998, the FDA approved Palivizumab (Synagis) for marketing for the prevention of serious lower respiratory tract disease caused by the respiratory syncytial virus (RSV) in pediatric patients at high risk of RSV disease.

On October 30, 2003, the FDA granted approval to use Palivizumab in young children < age 2 years, with hemodynamically significant CHD, to prevent serious lower respiratory tract infection or hospitalization caused by RSV.

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.

**Benefit Application:**
Coverage is subject to member’s specific benefits. Group specific policy will supersede this policy when applicable.

ITS: Home Policy provisions apply
BellSouth/AT&T contracts: Synagis is available through the Prescription Drug Program with Medco Health Solutions, Inc for all Health Plan Options administered by BCBSAL except the High Deductible Health Plan (HDHP) which BCBSAL in 2006 and 2007 only; for the HDHP, there were no special processing provisions for the coverage for Synagis and Regular business guidelines apply. For all Health Plan Options administered by BCBSAL in 2008, Synagis is available through Medco only. The HDHP is no longer administered by BCBSAL.
FEP contracts: Special benefit consideration may apply. Refer to member’s benefit plan.

**Lowe’s Precertification Requirement**—**Effective for dates of service on or after February 1, 2010** please contact Care Continuum at 866-240-4734 or fax the prescription with accompanying clinical information to 877-540-6223 for precertification. (This Blue Cross and Blue Shield of Alabama’s medical policy does not apply for Lowe’s members for dates of service on or after February 1, 2010). This policy was in effect for Lowe’s prior to February 1, 2010). Pre-certification requirements: Not applicable
Current Coding:
CPT Codes: 90378  Respiratory syncytial virus immune globulin (RSV-IGM) for intramuscular use, 50 mg, each

Effective for dates of service on or after January 1, 2010:
90378  Respiratory syncytial virus, monoclonal antibody, recombinant, for intramuscular use, 50 mg, each

Effective for dates of service on or after January 1, 2009:
96372  Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular

HCPCS: C9003  Palivizumab-RSV-IgM, per 50 mg (i.e., Synagis)

Previous Coding:
90379  Respiratory syncytial virus immune globulin (RSV-IGIV), human, for intravenous use (Code deleted effective January 1, 2010)
90765  Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour (Deleted effective January 1, 2009)
90766  ;each additional hour, up to 8 hours (list separately in addition to code for primary procedure) (Deleted effective January 1, 2009)
90772  Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular (Deleted effective January 1, 2009)
J1565  Injection, respiratory syncytial virus immune globulin, intravenous, 50 mg (i.e., RespiGam) (Code deleted effective January 1, 2010)

References:

**Policy History:**
Medical Policy Group, January 2007 (3)
Medical Policy Administration Committee, February 2007
Available for comment March 1-April 14, 2007
Medical Policy Group, October 2007 (3)
Medical Policy Administration Committee, October 2007
Available for comment October 20-December 3, 2007
Medical Policy Group, July 2009 (3)
Medical Policy Administration Committee, August 2009
Available for comment August 10-September 23, 2009
Medical Policy Group, October 2010 (1) Key Points updated, References updated; no changes to coverage statement
Medical Policy Group, May 2011 (3); Updated #6 in Policy section

Proprietary Information of Blue Cross and Blue Shield of Alabama
Medical Policy #302
Medical Policy Group, November 2012 (3): 2012 Updates to Description, Key Points, Governing Bodies, and References
Medical Policy Panel, August 2013
Medical Policy Group, August 2013 (3): 2013 Updates to Description, Key Points, and References; no change in policy statement
Medical Policy Group, October 2013 (3): Removed ICD-9 Procedure codes; no change to policy statement.
Medical Policy Group, October 2014 (1): Effective September 1, 2014 this policy will be maintained by PRIME. Please refer to the link at the top of this document for the proper policy.

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member’s plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield’s administration of plan contracts.