Bobby Jindal
GOVERNOR

Bruce D. Greenstein
SECRETARY

State of Louisiana

Department of Health and Hospitals

Office of the Secretary

September 13, 2010

Dear Pharmacist:

Re: Criteria for Reimbursement of Palivizumab (Synagis®) for the 2010-2011 RSV Season

The Louisiana Medicaid Pharmacy Benefits Management (LMPBM) Program has met with its Drug Utilization Review (DUR) Board and representatives from the Louisiana Chapter of the American Academy of Pediatrics (AAP) to update criteria for Medicaid reimbursement of palivizumab used for Respiratory Syncytial Virus (RSV) prophylaxis.

The LMPBM Program is reminding pharmacy providers of the following edits and limitations implemented by the LMPBM Program for palivizumab:

- Appropriate RSV Season
- Maximum number of doses allowed
- Appropriate age of recipient
- Appropriate diagnosis

The LMPBM Program will review pharmacy claims for adherence to program policy. Medicaid may request prescribing practitioners' records for patients receiving palivizumab and/or prescription copies for palivizumab to assure compliance with LMPBM Program policy.

We are pleased to enclose correspondence from the AAP authored by Dr. Stewart T. Gordon, President, Louisiana Chapter American Academy of Pediatrics and Dr. Joseph Bocchini, Jr., Chairman Department of Pediatrics at LSU Health Sciences Center-Shreveport. Dr. Bocchini is the immediate past chairman of the AAP Committee on Infectious Diseases. In addition, we are including the Policy Statement from the AAP regarding recommendations for palivizumab use for prevention of RSV.

If you have any concerns or comments regarding this correspondence, you may contact Melwyn B. Wendt, PharmD, at 225-342-9768 or send a fax to 225-342-1980. Your continued cooperation and support of the LMPBM Program are greatly appreciated.

Sincerely,

Don Gregory
Medicaid Director

DG/MJT/mbw

Enclosures

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

Louisiana Chapter

"To be advocates for all children in Louisiana"

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September 6, 2010

Rodney B. Wise, MD
Medicaid Medical Director
Louisiana Department of Health and Hospitals
628 N. 4th Street
P.O. Box 91030
Baton Rouge, LA 70821-9030

Dear Dr. Wise:

At the request of the DUR Board, the Louisiana Chapter of the American Academy of Pediatrics reviewed utilization considerations for palivizumab (Synagis®) at a recent DUR Board meeting. The data from the Centers for Disease Control and Prevention on the epidemiology of Respiratory Syncytial Virus (RSV) infections in Louisiana was also examined.

Payment parameters for Synagis® prescriptions established for the 2009-10 RSV season were based on the recommendations published by the American Academy of Pediatrics in 2009 (*Pediatrics* 2009;124:1694-1701). The full policy statement is available at: http://pediatrics.aappublications.org/cgi/reprint/124/6/1694.

We believe that the available evidence indicates that the guidelines developed last year resulted in improved identification of children who would most likely benefit from palivizumab administration while reducing use outside of the season when palivizumab would offer no significant benefit.

As we approach the 2010-2011 RSV season, the Louisiana Chapter of the AAP believes that prescribers should be aware of the following key points:

Synagis® prophylaxis is recommended from November through March for Louisiana.

Rationale:

Synagis® prophylaxis is recommended to protect at-risk infants during the annual seasonal RSV epidemic which occurs in Louisiana from November through March. There is some variability in the time of onset of the RSV season from year to year and within areas the state. Epidemiologic data collected over a number of years from monitoring sites within Louisiana and reported by the Centers for Disease Control and Prevention (CDC) indicate that although the onset each year may vary by a number of weeks, peak RSV activity is seen between December and March. Thus, based on the most data, the appropriate time for initiating Synagis® prophylaxis throughout Louisiana is at the 1st of November.

Sporadic cases of RSV will occur outside of the usual RSV season and are not an indication to initiate prophylaxis before November 1st. In addition, at the beginning of the season, when only a few RSV screening tests are being done, there is an increased likelihood that a positive test is a false positive. Also, when only a few tests are being performed, the percentage of positive tests is not an accurate indication of whether an RSV outbreak has begun. Therefore, decisions on altering the start date of prophylaxis should not be made based on only a few test results or results from a single local or regional laboratory. Any recommendation for change in onset or offset of RSV season will be based on CDC epidemiologic data and should come from State public health authorities.

The maximum number of Synagis® doses any recipient should receive is five (5). If a diagnosis code of 765.27 (33-34 completed weeks of gestation) is billed as the only indication for Synagis®, then a maximum of three (3) doses of Synagis® will be reimbursed.

Rationale:

Five doses of Synagis® provide protective serum concentrations of antibody for more than 20 weeks. Thirty days following administration of the 5th dose, many infants continue to have protective levels of antibody. The median duration of the RSV season has been 17 weeks or less according to CDC epidemiological data.

For infants 32 weeks 0 days through 34 weeks 6 days, born within 3 months before the start of the RSV season or during the RSV season, prophylaxis is recommended only if at least 1 of the following 2 risk factors is present: the infant attends child care (a home or facility in which care is provided for any number of infants or toddlers) or 1 or more siblings or other children younger than 5 years live permanently in the same household. These infants should receive a maximum of 3 monthly doses (up to 90 days of age).

Included in this packet is a copy of the 2009 AAP Policy Statement – Modified Recommendations for Use of Palivizumab for Prevention of Respiratory Syncytial Virus Infections. We would like to highlight two tables shown on pages 1697 and 1698 in the policy statement which can be helpful to providers when considering potential candidates for prophylaxis and for determining the number of doses indicated:

TABLE 2: Recommendations for the maximum number of doses of Synagis® based on indication

TABLE 3: A guide for determining the maximum number of doses for preterm infants without chronic lung disease of prematurity (formally: BPD) based on birth date, gestational age, and presence of risk factors with a prophylaxis starting date of November 1st.

Claims for Synagis® will only be reimbursed for recipients who are twenty-four (24) months of age and younger as of November 1st.

Rationale:

The two studies which led to FDA licensure of Synagis® were conducted in children 24 months of age or younger. Synagis® reduces the rate of lower respiratory tract disease associated with RSV infection which occurs primarily in children < 2 years old. Once a child qualifies for Synagis®, administration should continue throughout that RSV season and not stop when the child reaches 24 months of age.

There are ICD-9-CM diagnosis code requirements for reimbursement.

Rationale:

The decision to use Synagis® is based on gestational age, age at start of the RSV season and/or the presence of specific diagnoses. The decision to use Synagis® for certain diagnoses is subject to clinician assessment of risk factors and severity of underlying disease. For example, immunoprophylaxis with Synagis® for infants 32 weeks 0 days through 34 weeks 6 days depends on the presence of a risk factor (day care attendance or child < 5 years old in the household); for patients with congenital heart disease the decision is based on the degree of physiologic cardiovascular compromise; and for infants with neuromuscular conditions, on the degree to which the condition compromises the handling of respiratory secretions. The 2009 *Red Book* and the attached 2009 AAP Policy Statement provide detailed information regarding Synagis® use.

The Louisiana Chapter of the AAP appreciates this opportunity to work together to improve the care of the children of Louisiana. By basing palivizumab utilization considerations on evidence-based criteria we will provide more cost-effective care to our patients. We are also happy to be of assistance to you in updating physician knowledge of the recently published AAP recommendations.

If we can aid you in any other way, please contact us.

Sincerely,

Stewart T. Gordon, M.D.

Stewart Gordon, MD
President
Louisiana Chapter American Academy of Pediatrics

Joseph A. Bocchini, Jr., MD
Immediate Past Chairman
AAP Committee on Infectious Diseases

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Policy Statement—Modified Recommendations for Use of Palivizumab for Prevention of Respiratory Syncytial Virus Infections

COMMITTEE ON INFECTIOUS DISEASES

KEY WORDS
RSV bronchiolitis, palivizumab, immunoprophylaxis

ABBREVIATIONS
COC—Centers for Disease Control and Prevention
RSV—respiratory syncytial virus
CHD—congenital heart disease
CLD—chronic lung disease of prematurity

Palivizumab was licensed in June 1998 by the US Food and Drug Administration for prevention of serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) in pediatric patients who are at increased risk of severe disease. Safety and efficacy have been established for infants born at or before 35 weeks' gestation with or without chronic lung disease of prematurity and for infants and children with hemodynamically significant heart disease. The American Academy of Pediatrics (AAP) published a policy statement on the use of palivizumab in November 1998 (American Academy of Pediatrics, Committee on Infectious Diseases and Committee on Fetus and Newborn. *Pediatrics*. 1998;102[5]:1211–1216) and revised it in December 2003 (American Academy of Pediatrics, Committee on Infectious Diseases and Committee on Fetus and Newborn. *Pediatrics*. 2003;112[6 pt 1]:1442–1446), and an AAP technical report on palivizumab was published in 2003 (Meissner HC, Long SS; American Academy of Pediatrics, Committee on Infectious Diseases and Committee on Fetus and Newborn. *Pediatrics*. 2003;112[6 pt 1]:1447–1452). On the basis of the availability of additional data regarding seasonality of RSV disease as well as the limitations in available data on risk factors for identifying children who are at increased risk of serious RSV lower respiratory tract disease, AAP recommendations for immunoprophylaxis have been updated in an effort to ensure optimal balance of benefit and cost from this expensive intervention. This statement updates and replaces the 2003 AAP statement and the 2006 *Red Book* and is consistent with the 2009 *Red Book* recommendations. *Pediatrics* 2009;124:1694–1701

www.pediatrics.org/cgi/doi/10.1542/peds.2009-2345
doi:10.1542/peds.2009-2345

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

SUMMARY

1. Recommendations for initiation and termination of prophylaxis are modified to reflect current descriptions from the Centers for Disease Control and Prevention (CDC) of respiratory syncytial virus (RSV) seasonality in different geographic locations within the United States.
2. The recommendations remain unchanged for infants with congenital heart disease (CHD), chronic lung disease of prematurity (CLD [formerly called bronchopulmonary dysplasia]), and birth before 32 weeks' 0 days' gestation.
3. Regardless of the month in which the first dose is administered, the recommendation for a maximal number of 5 doses for all geo-

graphic locations is emphasized for infants with hemodynamically significant CHD, CLD, or birth before 32 weeks' 0 days' gestation. A maximal number of 3 doses is recommended for infants with a gestational age of 32 weeks 0 days to 34 weeks 6 days without hemodynamically significant CHD or CLD who qualify for prophylaxis.

4. Because of inconsistencies among studies that attempted to define risk factors identifying children at greatest risk of serious RSV lower respiratory tract disease, the new recommendations were designed to target children at the highest risk of severe disease with risk factors that are most consistent and predictive. Risk factors for severe disease among infants born between 32 weeks' 0 days' and 34 weeks' 6 days' gestation have been modified to include only:
   a. infant attends child care; or
   b. 1 or more siblings or other children younger than 5 years live permanently in the child's household.
5. Infants with a gestational age of 32 weeks 0 days through 34 weeks 6 days born within 3 months before the start of RSV season or at any time throughout the RSV season will qualify for prophylaxis under the new recommendations if they have at least 1 of these 2 risk factors. Previous recommendations required 2 of 5 risk factors.
6. Infants born from 32 weeks' 0 days' through 34 weeks' 6 days' gestation who qualify for prophylaxis under the new recommendations should receive prophylaxis only until they reach 90 days of age or a maximum of 3 doses (whichever comes first). This is a change from the previous recommendation for 5 months of prophylaxis.
7. The American Academy of Pediatrics 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. The previous definition was 32 weeks 1 day through 35 weeks 0 days.

BACKGROUND

RSV is an enveloped, nonsegmented, negative-strand RNA virus of the family *Paramyxoviridae*. The virus uses attachment (G) and fusion (F) surface glycoproteins that lack neuraminidase and hemagglutinin activities to infect cells. RSV causes acute upper respiratory tract infection in patients of all ages and is one of the most common diseases of childhood. Most infants are infected during their first year of life, with virtually all children having been infected at least once by their second birthday. A minority of patients experience lower respiratory tract disease, which occurs most commonly during the first infection. Characteristics that increase the risk of severe RSV lower respiratory tract illness are preterm birth; cyanotic or complicated CHD, especially conditions that cause pulmonary hypertension; and CLD. RSV bronchiolitis may be associated with short-term or long-term complications that include recurrent wheezing, reactive airway disease, and abnormalities in pulmonary function. Reinfection with RSV throughout life is common. RSV infection in older children and adults usually manifests as upper respiratory tract illness. More serious disease involving the lower respiratory tract may develop in older children and adults, especially immunocompromised patients and the elderly, particularly those with cardiopulmonary disease. RSV causes the hospitalization of approximately 57 500 children younger than 5 years annually and is estimated to account for 1 of every 334 hospitalizations in this age group each year.[1]

Prevention of RSV Infections

Palivizumab is the only licensed product available for prevention of RSV lower respiratory tract disease in infants and children with CLD, with a history of preterm birth (≤35 weeks' gestation), or with hemodynamically significant CHD. Palivizumab is a humanized murine monoclonal anti-F glycoprotein immunoglobulin with neutralizing and fusion inhibitory activity against RSV.[2] Palivizumab is administered intramuscularly at a dose of 15 mg/kg once every 30 days. An attempt should be made to maintain compliance with monthly administration. In some reports, palivizumab administration in a home-based program was shown to improve compliance and reduce children's risk of exposure to microbial pathogens compared with administration in office- or clinic-based settings.[3] Additional doses of palivizumab should not be given to any patient with a history of a severe allergic reaction after a previous dose. Palivizumab is not effective in the treatment of RSV disease and is not approved or recommended for this indication.

RSV immunoglobulin intravenous (RSV-IgIV), a hyperimmune, polyclonal globulin prepared from donors selected for high serum titers of RSV-neutralizing antibody, is no longer available.

Clinical Studies of Efficacy of Palivizumab

The efficacy of palivizumab has been evaluated in 2 multicenter, placebo-controlled, randomized clinical trials, both of which used a primary end point of reduction in hospitalization attributable to RSV infection. The RSV-IMpact trial evaluated children 24 months of age or younger with CLD who required continuing medical therapy (supplemental oxygen, bronchodilator, or diuretic or corticosteroid therapy within the previous 6 months) and children

born at 35 weeks' gestation or less who were 6 months of age or younger at the start of the RSV season.[4] Prophylaxis resulted in a 55% overall decrease in the rate of RSV-related hospitalization (10.6% and 4.8% in recipients of placebo versus palivizumab, respectively [$P < .001$]). A second study of infants and children with hemodynamically significant CHD demonstrated a 45% decrease in the rate of RSV-related hospitalization (9.7% and 5.3% in recipients of placebo versus palivizumab, respectively [$P = .003$]).[5] Among different groups of infants at high risk, hospitalization rates attributable to RSV were reduced by 39% to 82%, relative to control groups.[4,5]

Cost Considerations

Immunoprophylaxis with palivizumab is an effective, although costly, intervention. Optimal cost benefit from immunoprophylaxis is achieved during the peak outbreak months, in which most RSV hospitalizations occur. If prophylaxis is initiated after widespread RSV circulation has begun, infants at high risk may not receive the full benefit of protection. Conversely, early initiation or continuation of monthly immunoprophylaxis during months in which RSV is not circulating widely is not cost-effective and provides little benefit to the recipients.[6]

The primary benefit of immunoprophylaxis is a decrease in the rate of RSV-associated hospitalization. No prospective, randomized clinical trial has demonstrated a significant decrease in the rate of mortality attributable to RSV or in the rate of recurrent wheezing after RSV infection among infants who receive prophylaxis.[7] Economic analyses have failed to demonstrate overall savings in health care dollars because of the high cost if all infants who are at risk receive prophylaxis.[8–14]

Initiation and Termination of Immunoprophylaxis

In the temperate climates of North America, peak RSV activity typically occurs between November and March, whereas in equatorial countries, RSV seasonality patterns vary and may occur throughout the year. The inevitability of the RSV season is predictable, but the severity of the season, the time of onset, the peak of activity, and end of the season cannot be predicted precisely. Substantial variation in the timing of community outbreaks of RSV disease from year to year exists within and between communities in the same year, even in the same region. These variations occur within the overall pattern of RSV outbreaks, usually beginning in November or December, peaking in January or February, and ending by the end of March or sometime in April. Communities in the southern United States, particularly some communities in the state of Florida, tend to experience the earliest onset of RSV activity. In recent years, the national median duration of the RSV season has been 17 weeks or less.[15,16] Results from clinical trials indicate that palivizumab trough serum concentrations greater than 30 days after the fifth dose will be well above the protective concentration for most infants, thus providing more than 20 weeks of protective serum antibody concentration. In the continental United States, a total of 5 monthly doses for infants and young children with CHD, CLD, or preterm birth before 32 weeks' gestation (31 weeks 6 days) will provide an optimal balance of benefit and cost, even with variation in the season's onset and end (AI; see Appendix).

For infants who qualify for 5 doses, initiation of immunoprophylaxis in November and continuation for a total of 5 monthly doses will provide protection into April and is recommended for most areas of the United States. If prophylaxis is initiated in October, the fifth and final dose should be administered in February (BI).

Data from the CDC have identified variations in the onset and offset of the RSV season in the state of Florida that should affect the timing of palivizumab administration (CDC, unpublished data, 2008; and refs 16 and 17). Northwest Florida has an onset in mid-November, which is consistent with other areas of the United States. In north central and southwest Florida, the onset of RSV season typically is late September to early October. The RSV season in southeast Florida (Miami-Dade County) typically has its onset in July. Despite varied onsets, the RSV season is of equal duration in the different regions of Florida. Children who qualify for palivizumab prophylaxis for the entire RSV season (infants and children with CLD, CHD, or preterm birth born before 32 weeks' gestation) should receive palivizumab administration only during the 5 months after the onset of RSV season in their region (maximum of 5 doses), which should provide coverage during the peak of the season, when prophylaxis is most effective (Table 1) (BIII).

Specific groups of American Indian/Alaska Native children in certain geographic regions may experience more severe RSV disease and a longer RSV season. RSV hospitalizations for Navajo and White Mountain Apache infants and young children may be 2 to 3 times those of similarly aged children in the general US population.[18] How-

TABLE 1 Palivizumab Prophylaxis for Infants and Young Children With CLD or CHD

Geographic Location	Earliest Date for Initiation of 5 Monthly Doses
Southeast Florida	Jul 1
North-central and southwest Florida	Sep 15
Most other areas of United States	Nov 1

TABLE 2 Maximum Number of Monthly Doses of Palivizumab for RSV Prophylaxis

Infants Eligible for a Maximum of 5 Doses	Infants Eligible for a Maximum of 3 Doses
Infants with CLD, <24 mo of age, and require medical therapy	Premature infants with a gestational age of 32 wk 0 d to 34 wk 6 d with at least 1 risk factor and born 3 mo before or during RSV season
Infants with CHD, <24 mo of age, and require medical therapy	
Premature infants born at ≤31 wk 6 d	
Certain infants with neuromuscular disease or congenital abnormalities of the airways	

ever, the timing and duration of the RSV season is similar to those in the remainder of the United States (November through March), so standard recommendations for infants and children with CHD, CLD, or preterm birth (before 32 weeks' gestation) still are appropriate. Alaska Native infants in southwestern Alaska experience not only higher RSV hospitalization rates but also a longer RSV season. Pediatricians in this area of Alaska may wish to use CDC-generated RSV hospitalization data to assist in determining the onset and offset of the RSV season for the appropriate timing of palivizumab administration[19] (BII).

Infants and children with CHD, CLD, or birth before 32 weeks' 0 days' gestation who initiate palivizumab prophylaxis after start of the RSV season will not require all 5 doses (Table 2) (AI).

Eligibility Criteria for Prophylaxis of Infants and Young Children at High Risk

- Infants with CLD: Palivizumab prophylaxis may be considered for infants and children younger than 24 months with CLD who receive medical therapy (supplemental oxygen, bronchodilator, diuretic or chronic corticosteroid therapy) for CLD within 6 months before the start of the RSV season. These infants and young children should receive a maximum of 5 doses. Patients with the most severe CLD who continue to require medical therapy may benefit from prophylaxis during a second RSV season. Data are limited regarding the effectiveness of palivizumab during the second year of life. Individual patients may benefit from decisions made in consultation with neonatologists, pediatric intensivists, pulmonologists, or infectious disease specialists (AI).
- Infants born before 32 weeks' gestation (≤31 weeks 6 days): Infants in this category may benefit from RSV prophylaxis even if they do not have CLD. For these infants, major risk factors to consider include gestational age and chronologic age at the start of the RSV season. Infants born at 28 weeks' gestation or earlier may benefit from prophylaxis during the RSV season whenever that occurs during the first 12 months of life. Infants born at 29 to 32 weeks' gestation (≤31 weeks 6 days) may benefit most from prophylaxis up to 6 months of age. However, once an infant qualifies for initiation of prophylaxis at the start of the RSV season, administration should continue throughout the season and not stop when the infant reaches either 6 or 12 months of age. A maximum of 5 monthly doses are recommended for infants in this category (AI).
- Infants born at 32 to less than 35 weeks' gestation (defined as 32 weeks 0 days through 34 weeks 6 days): Numerous factors have been proposed as increasing the risk of acquiring RSV infection among infants in this gestational-age group. Other factors have been associated with an increased risk of severe disease and hospitalization. Certain factors (CHD, prematurity, CLD) are well-established risk factors for hospitalization, because they consistently are present in various studies. In contrast, other reported risk factors either are found inconsistently, even in studies by the same authors, or increase the risk of hospitalization by a relatively small factor (less than twofold to threefold). A risk-scoring tool developed from a Canadian prospective study of infants born at 33 through 35 weeks' gestation revealed that multiple risk factors needed to be present before a significant increase in hospitalization risk was seen.[20] In addition, available data do not enable definition of a subgroup of infants who are at risk of prolonged hospitalization and admission to the ICU. Therefore, although current recommendations were designed to be consistent with the US Food and Drug Administration approval for marketing of palivizumab for the prevention of serious RSV lower respiratory track disease, they specifically target infants in this group with consistently identified risk factors for RSV hospitalization during the period of greatest risk, which is the first 3 months of life.[21–28] Palivizumab prophylaxis should be limited to infants in this group at greatest risk of hospitalization attributable to RSV, namely infants younger than 3 months of age at the start of the RSV season and infants born during the RSV season who are likely to have an increased risk of exposure to RSV. Epidemiologic data suggest that RSV infection is more likely to occur and more likely to lead to hospitalization for infants in this gestational-age group when at least 1 of the following 2 risk factors is present:

Maximum Number of Palivizumab Doses for RSV Prophylaxis of Preterm Infants Without CLD, Based on Birth Date, Gestational Age, and Presence of Risk Factors (Shown for Areas Beginning Prophylaxis on November 1st)

Month of Birth	Maximum No. of Doses for Season Beginning Nov 1		
	≤28 wk 6 d Gestation and <12 mo of Age at Start of Season	29 wk 0 d Through 31 wk 6 d Gestation and <6 mo of Age at Start of Season	32 wk 0 d Through 34 wk 6 d and With Risk Factor[a]
Nov 1–Mar 31 of previous RSV season	5[b]	0[c]	0[d]
Apr	5	0[c]	0[d]
May	5	5	0[d]
Jun	5	5	0[d]
Jul	5	5	0[d]
Aug	5	5	1[e]
Sep	5	5	2[e]
Oct	5	5	3[e]
Nov	5	5	3[e]
Dec	4	4	3[e]
Jan	3	3	3[e]
Feb	2	2	2[e]
Mar	1	1	1[e]

If the infant is discharged from the hospital during RSV season, fewer doses may be required.

[a] Risk factors: infant attends child care or has sibling younger than 5 years.

[b] Some of these infants may have received 1 or more doses of palivizumab in the previous RSV season if discharged from the hospital during that season; if so, they still qualify for up to 5 doses during their second RSV season.

[c] Zero doses because infant will be older than 6 months at the start of RSV season.

[d] Zero doses because infant will be older than 90 days of age at start of RSV season.

[e] On the basis of the age of patients at the time of discharge from the hospital, fewer doses may be required, because these infants will receive 1 dose every 30 days until the infant is 90 days of age.

- the infant attends child care, defined as a home or facility in which care is provided for any number of infants or toddlers in the child care facility; or
- 1 or more siblings or other children younger than 5 years live permanently in the same household.

Prophylaxis may be considered for infants from 32 through less than 35 weeks' gestation (defined as 32 weeks 0 days through 34 weeks 6 days) who are born less than 3 months before the onset or during the RSV season and for whom at least 1 of the 2 risk factors is present. Infants in this gestational-age category should receive prophylaxis only until they reach 3 months of age and should receive a maximum of 3 monthly doses; many will receive only 1 or 2 doses before they reach 3 months of age. Once an infant has passed 90 days of age, the risk of hospitalization attributable to RSV lower respiratory tract disease is reduced. Administration of palivizumab is not recommended after 90 days of age (Tables 2 and 3) (BIII).

Infants, especially those at high risk, never should be exposed to tobacco smoke. Tobacco smoke is a known risk factor for many adverse health-related outcomes.[29] However, in published studies, passive household exposure to tobacco smoke has not been associated with an increased risk of RSV hospitalization on a consistent basis. Exposure to tobacco smoke must be controlled by families with infants, especially with infants who are at increased risk of RSV disease. Such preventive measures will be far less costly than palivizumab prophylaxis.

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.[30] Infants at high risk 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 infants at high risk whenever feasible. Parents should be instructed on the importance of careful hand hygiene. In addition, all infants (beginning at 6 months of age) and their contacts (beginning when the child is born) should receive influenza vaccine as well as other recommended age-appropriate immunizations.

- Infants with congenital abnormalities of the airway or neuromuscular disease: Immunoprophylaxis may be considered for infants who have either significant congenital abnormalities of the airway or a neuromuscular condition that compromises handling of respiratory tract secretions. Infants and young children in this category should receive a maximum of 5 doses of palivizumab during the first year of life (CIII).
- Infants and children with CHD: Children who are 24 months of age or younger with hemodynamically significant cyanotic or acyanotic CHD may benefit from palivizumab prophylaxis.[5] Decisions regarding prophylaxis with palivizumab in children with CHD should be made on the basis of the degree of physiologic cardiovascular compromise. Children younger than 24 months of age with CHD who are most likely to benefit from immunoprophylaxis include:
  - infants who are receiving medication to control congestive heart failure;

- infants with moderate-to-severe pulmonary hypertension; and
- infants with cyanotic heart disease.

Because a mean decrease in palivizumab serum concentration of 58% was observed after surgical procedures that use cardiopulmonary bypass, for children who continue to require prophylaxis, a postoperative dose of palivizumab (15 mg/kg) should be administered as soon as the patient is medically stable (AI).

The following groups of infants with CHD are not at increased risk of RSV and generally should not receive immunoprophylaxis:

- Infants and children 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);
- Infants with lesions adequately corrected by surgery, unless they continue to require medication for congestive heart failure; and
- Infants with mild cardiomyopathy who are not receiving medical therapy for the condition.

Dates for initiation and termination of prophylaxis should be based on the same considerations as those for high-risk infants with CLD.

- Immunocompromised children: Palivizumab prophylaxis has not been evaluated in randomized trials in immunocompromised children. Although specific recommendations for immunocompromised children cannot be made, infants and young children with severe immunodeficiency (eg, severe combined immunodeficiency or advanced AIDS) may benefit from prophylaxis (CIII).
- Patients with cystic fibrosis: Limited studies suggest that some patients with cystic fibrosis may be at increased risk of RSV infection. Whether RSV infection exacerbates the chronic lung disease of cystic fibrosis is not known. In addition, insufficient data exist to determine the effectiveness of palivizumab use in this patient population.[31] Therefore, a recommendation for routine prophylaxis in patients with cystic fibrosis cannot be made (CIII).
- Special situations
  - If an infant or child who is receiving palivizumab immunoprophylaxis experiences a breakthrough RSV infection, monthly prophylaxis should continue until a maximum number of 3 doses have been administered to infants in the 32 weeks' 0 days' through 34 weeks' 6 days' gestational-age group or until a maximum of 5 doses have been administered to infants with CHD, CLD, or preterm birth before 32 weeks' gestation. This recommendation is based on the observation that infants at high risk may be hospitalized more than once in the same season with RSV lower respiratory tract disease and the fact that more than 1 RSV strain often cocirculates in a community (CIII).
  - Hospitalized infants who qualify for prophylaxis during the RSV season should receive the first dose of palivizumab 48 to 72 hours before discharge or promptly after discharge (CIII).
  - Infants who have begun palivizumab prophylaxis earlier in the season and are hospitalized on the date when the next monthly dose is due should receive that dose as scheduled while they remain in the hospital (AI).
  - RSV is known to be transmitted in the hospital setting and to cause serious disease in infants at high risk. Among hospitalized infants, the major means of reducing RSV transmission is strict observance of infection-control practices, including prompt initiation of precautions for RSV-infected infants.[32] If an RSV outbreak occurs in a high-risk unit (eg, PICU or NICU or stem cell transplantation unit), primary emphasis should be placed on proper infection-control practices, especially hand hygiene. No data exist to support palivizumab use in controlling outbreaks of health care–associated disease, and palivizumab use is not recommended for this purpose (CIII).
  - Palivizumab does not interfere with response to vaccines.

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APPENDIX Infectious Diseases Society of America–US Public Health Service Grading System for Ranking Recommendations in Clinical Guidelines

Category, Grade	Definition
Strength of recommendation	
A	Good evidence to support a recommendation for use
B	Moderate evidence to support a recommendation for use
C	Poor evidence to support a recommendation
Quality of evidence	
I	Evidence from ≥1 properly randomized, controlled trial
II	Evidence from ≥1 well-designed clinical trial, without randomization; from cohort or case-controlled analytical studies (preferably from >1 center); from multiple time series; or from dramatic results from uncontrolled experiments
III	Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

Adapted from Canadian Task Force on the Periodic Health Examination. *Can Med Assoc J*. 1979;121(9):1193–1254.

Palivizumab (Synagis®) Reimbursement Criteria for the 2010-2011

Palivizumab is indicated for the prevention of serious lower respiratory tract infection caused by respiratory syncytial virus (RSV) in selected infants and young children. The Louisiana Medicaid Pharmacy Benefits Management (LMPBM) Program has established criteria for reimbursement of palivizumab. The LMPBM Program criteria are based on recommendations from the Louisiana Medicaid Drug Utilization Review (DUR) Board and on the American Academy of Pediatrics (AAP) *Policy Statement—Modified Recommendations for Use of Palivizumab for Prevention of Respiratory Syncytial Virus Infections.* An electronic copy of the AAP policy statement is available at http://pediatrics.aappublications.org/cgi/reprint/124/6/1694 .

Pharmacy claims for palivizumab will be reimbursed by Louisiana Medicaid when prescriptions meet all of the following five (5) criteria:

RSV Season

- Palivizumab claims will be reimbursed in accordance with an RSV Season of November 1, 2010 through March 31, 2011.
- Louisiana RSV activity may be followed during the RSV Season by accessing http://www.cdc.gov/surveillance/nrevss/rsv/state.html .

Maximum Number of Doses Allowed

- Based upon the diagnosis code submitted, a maximum of five (5) doses of palivizumab will be reimbursed each RSV Season.
- **If a diagnosis code of 765.27 (33-34 completed weeks of gestation) is submitted, then a maximum of three (3) doses will be reimbursed each RSV Season.**

Age Restriction

- Palivizumab claims will be reimbursed for recipients who are twenty-four (24) months of age and younger as of November 1, 2010.

ICD-9-CM Diagnosis Code Requirement

- An ICD-9-CM diagnosis code to justify the reason for palivizumab use must be documented on all palivizumab prescriptions.
- The ICD-9-CM diagnosis codes which are in accordance with the reimbursement criteria are based on the AAP Policy Statement *and* DUR Board recommendations regarding palivizumab use.
- Two lists containing ICD-9-CM diagnosis codes which are in accordance with the reimbursement criteria are provided:
  - List 1 – Diagnoses Which Justify Palivizumab Use
  - List 2 – Diagnoses Which May Justify Palivizumab Use Depending on Recipient-Specific Factors
- Claims for palivizumab shall be submitted with one (1) of the diagnosis codes in List 1 or List 2 entered in **NCPDP field 424-DO (Diagnosis Code).**

Early Refill

- Palivizumab claims will process for payment every twenty-eight (28) days.

Palivizumab Use Outside the Reimbursement Criteria

- A palivizumab prescription which does not meet all the reimbursement criteria must be handwritten and signed by the prescribing practitioner. Signature stamps and proxy signatures are not acceptable.
- Palivizumab use that does not meet all reimbursement criteria requires **a handwritten hardcopy prescription with (1) a justification for use outside the criteria and (2) an ICD-9-CM diagnosis code handwritten by the prescribing practitioner.** The justification provided should also be documented in the recipient's medical record. The handwritten prescription, justification, and ICD-9-CM diagnosis code are necessary for the pharmacy to override the claim denial.
- This prescription may be faxed to the pharmacy and must be retained by the pharmacy for audit review.
- Medical records may be requested for verification of palivizumab claims submitted outside the reimbursement criteria.
- In order to facilitate availability of palivizumab to home health providers for administration in November, Medicaid will allow transmittal of palivizumab claims through the electronic Point of Sale system beginning October 18, 2010.

Overriding a Denied Palivizumab Claim

Respiratory Syncytial Virus (RSV) Season

- A claim submitted for palivizumab outside the 'RSV Season' criterion requires a **handwritten hardcopy prescription with (1) a justification for use outside the criterion and (2) an ICD-9-CM diagnosis code handwritten by the prescribing practitioner.** This prescription may be faxed to the pharmacy and must be retained by the pharmacy for audit review.

- A palivizumab claim with a date of service outside of the RSV Season will deny with:

  NCPDP rejection code 88 (DUR Reject Error)
  mapped to EOB code 656 (Exceeds Maximum Duration of Therapy).

  Override: After consultation with the prescribing practitioner and receipt of a handwritten hardcopy prescription with (1) a justification for use of palivizumab outside the RSV Season and (2) an ICD-9-CM diagnosis code handwritten by the prescribing practitioner, the pharmacist may override the 'RSV Season' criterion. The pharmacist must have the justification and an ICD-9-CM diagnosis code from the prescribing practitioner and document the codes listed below and submit the override with:

  NCPDP 439-E4 field (Reason for Service Code)-MX (Exceeds Maximum Duration)
  NCPDP 440-E5 field (Professional Service Code)-MØ (Prescriber Consulted)
  NCPDP 441-E6 field (Result of Service Code)-1G (Filled with Prescriber Approval)

- Medical records may be requested for verification purposes of a pharmacy claim submitted for palivizumab outside the five (5) month RSV Season.

Maximum Number of Doses Allowed

- Counting of palivizumab doses will begin with a recipient's first palivizumab claim associated with a date of service on or after October 18, 2010.

- A claim submitted for palivizumab outside the 'Maximum Number of Doses Allowed' criterion requires **a handwritten hardcopy prescription with (1) a justification for use outside the criterion and (2) an ICD-9-CM diagnosis code handwritten by the prescribing practitioner.** This prescription may be faxed to the pharmacy and must be retained by the pharmacy for audit review.

- A claim submitted for palivizumab outside the maximum number of doses allowed will deny with:

  NCPDP rejection code 88 (DUR Reject Error)
  mapped to EOB code 656 (Exceeds Maximum Duration of Therapy).

  Override: After consultation with the prescribing practitioner and receipt of a handwritten hardcopy prescription with (1) a justification for use of palivizumab outside the maximum number of doses allowed and (2) an ICD-9-CM diagnosis code handwritten by the prescribing practitioner, the pharmacist may override the 'Maximum Number of Doses Allowed' criterion. The pharmacist must have the justification and an ICD-9-CM diagnosis code from the prescribing practitioner and document the codes listed below and submit the override with:

  NCPDP 439-E4 field (Reason for Service Code)-MX (Exceeds Maximum Duration)
  NCPDP 440-E5 field (Professional Service Code)-MØ (Prescriber Consulted)
  NCPDP 441-E6 field (Result of Service Code)-1G (Filled with Prescriber Approval)

- Medical records may be requested for verification purposes of a pharmacy claim submitted for palivizumab doses in excess of the maximum number of doses allowed.

Age Restriction

- A claim submitted for palivizumab outside the 'Age Restriction' criterion requires **a handwritten hardcopy prescription with (1) a justification for use outside the criterion and (2) an ICD-9-CM diagnosis code handwritten by the prescribing practitioner.** This prescription may be faxed to the pharmacy and must be retained by the pharmacy for audit review.

- A claim submitted for palivizumab for a recipient who is twenty-five (25) months of age or older on November 1, 2010, will deny with:

  NCPDP rejection code 60 (Product/Service Not Covered for Patient Age)
  mapped to EOB code 234 (P/F Age Restriction).

  Override: After consultation with the prescribing practitioner and receipt of a handwritten hardcopy prescription with (1) a justification for use of palivizumab outside the age restriction and (2) an ICD-9-CM diagnosis code handwritten by the

prescribing practitioner, the pharmacist may override the 'Age Restriction' criterion. The pharmacist must have the justification and an ICD-9-CM diagnosis code from the prescribing practitioner and document the codes listed below and submit the override with:

NCPDP 439-E4 field (Reason for Service Code)-PA (Drug-Age)
NCPDP 440-E5 field (Professional Service Code)-MØ (Prescriber Consulted)
NCPDP 441-E6 field (Result of Service Code)-1G (Filled with Prescriber Approval)

- Medical records may be requested for verification purposes of a pharmacy claim submitted for palivizumab outside the age restriction.

ICD-9-CM Diagnosis Code Requirement

- A claim submitted for palivizumab that does not include an ICD-9-CM diagnosis code from List 1 or List 2 requires **a handwritten hardcopy prescription with (1) a justification for use outside the criterion and (2) an ICD-9-CM diagnosis code handwritten by the prescribing practitioner.** This prescription may be faxed to the pharmacy and must be retained by the pharmacy for audit review.

- A palivizumab claim either submitted with an ICD-9-CM diagnosis code which is not in List 1 or List 2 or submitted without any diagnosis code will deny with:

  NCPDP rejection code 39 (Missing or Invalid Diagnosis Code)
  mapped to EOB code 575 (Missing or Invalid Diagnosis Code).

  Override: After consultation with the prescribing practitioner and receipt of a handwritten hardcopy prescription with (1) a justification for use of palivizumab outside the diagnosis code requirement and (2) an 'alternative' ICD-9-CM diagnosis code handwritten by the prescribing practitioner, the pharmacist may override the 'Diagnosis Code' criterion. The pharmacist must have the justification and an ICD-9-CM diagnosis code from the prescribing practitioner and document the codes listed below and submit the override by:

  Placing the 'alternative' ICD-9-CM diagnosis code in NCPDP field 424-DO (Diagnosis Code) and by placing '03' in NCPDP 418-DI field (Level of Service).

- Medical records may be requested for verification purposes of a pharmacy claim submitted for palivizumab associated with a diagnosis not in List 1 or List 2 or for a pharmacy claim submitted without a diagnosis code.

Early Refill

- A claim submitted for palivizumab outside the 'Early Refill' criterion requires **a handwritten hardcopy prescription with (1) a justification for use outside the criterion and (2) an ICD-9-CM diagnosis code handwritten by the prescribing practitioner.** This prescription may be faxed to the pharmacy and must be retained by the pharmacy for audit review.

- A claim for palivizumab processed for payment earlier than every twenty-eight (28) days will deny.

- When a pharmacy submits a claim for palivizumab and the same pharmacy previously submitted the active prescription, the incoming claim will deny with:

  NCPDP rejection code 88 (DUR Reject Error)
  mapped to EOB 447 (Compliance Monitoring/Early or Late Refill).

Note: An active prescription is a prescription for which the days supply has not expired.

Override: After consultation with the prescribing practitioner and receipt of a handwritten hardcopy prescription with (1) a justification for use of palivizumab earlier than every 28 days and (2) an ICD-9-CM diagnosis code handwritten by the prescribing practitioner, the pharmacist may override the 'Early Refill' criterion. The pharmacist must have the justification for the early fill date and an ICD-9-CM diagnosis code from the prescribing practitioner and document the codes listed below and submit the override with:

NCPDP 439-E4 field (Reason for Service Code)-ER (Overuse/Early Refill)
NCPDP 440-E5 field (Professional Service Code)-MØ (Prescriber Consulted)
NCPDP 441-E6 field (Result of Service Code)-1G (Filled with Prescriber Approval)

- When a pharmacy submits a claim for palivizumab and another pharmacy has previously submitted the active prescription, the incoming claim will deny with:

  NCPDP rejection code 88 (DUR Reject Error)
  mapped to EOB 445 (Duplicate Drug Therapy).

Override: After consultation with the prescribing practitioner and receipt of a handwritten hardcopy prescription with (1) a justification for use of palivizumab earlier than every 28 days and (2) an ICD-9-CM diagnosis code handwritten by the prescribing practitioner, the pharmacist may override the 'Early Refill' criterion. The pharmacist must have the justification for the early fill date and an ICD-9-CM diagnosis code from the prescribing practitioner and document the codes listed below and submit the override with:

NCPDP 439-E4 field (Reason for Service Code)-ID (Ingredient Duplication)
NCPDP 440-E5 field (Professional Service Code)-MØ (Prescriber Consulted)
NCPDP 441-E6 field (Result of Service Code)-1G (Filled with Prescriber Approval)

- Medical records may be requested for verification purposes of a pharmacy claim submitted for palivizumab outside the 'Early Refill' criterion.

ICD-9-CM Diagnosis Codes in Accordance with Reimbursement Criteria

List 1: Diagnoses Which Justify Palivizumab Use

ICD-9-CM Diagnosis Code	Description
415.0	Acute cor pulmonale
416.0	Primary pulmonary hypertension
416.8	Pulmonary hypertension, secondary
745.0	Truncus arteriosus
745.10-745.11	Transposition of the great vessels
745.19	Other transposition of the great vessels
745.2	Tetralogy of Fallot
746.1	Tricuspid atresia and stenosis, congenital
746.2	Ebstein's anomaly
747.41	Total anomalous pulmonary venous return
747.83	Persistent pulmonary hypertension, primary pulmonary hypertension of the newborn (Persistent fetal circulation)
765.21	Less than 24 completed weeks of gestation
765.22	24 completed weeks of gestation
765.23	25-26 completed weeks of gestation
765.24	27-28 completed weeks of gestation
765.25	29-30 completed weeks of gestation
765.26	31-32 completed weeks of gestation
765.27	33-34 completed weeks of gestation
770.7	Chronic respiratory disease arising in perinatal period (CLD/BPD/interstitial pulmonary fibrosis of infancy/ Wilson-Mikity Syndrome)

List 2: Diagnoses Which May Justify Palivizumab Use Depending on Recipient-Specific Factors

ICD-9-CM Diagnosis Code	Description
042	Human immunodeficiency virus (HIV) disease
045.00-045.13	Infantile paralysis
277.00-277.09	Cystic fibrosis
279.00-279.90	Disorders involving the immune system
335.0	Werdnig-Hoffman disease
335.10-335.11	Spinal muscular atrophy
335.20-335.24	Motor neuron disease
343.0-343.9	Infantile cerebral palsy
358.0-358.9	Myoneural disorders
359.0-359.9	Muscular dystrophies and other myopathies
396.0-396.9	Diseases of mitral and aortic valves
424.1	Aortic stenosis
425.00-425.90	Cardiomyopathy
428.0-428.9	Heart failure
519.1	Other diseases of the trachea and bronchus, not elsewhere classified (Must specify tracheomalacia or tracheal stenosis.)
745.4	Ventricular septal defect
745.5	Atrial septal defect
745.60-745.69	Atrioventricular canal (endocardial cushion defect)
746.7	Hypoplastic left heart
746.89	Hypoplastic right heart
748.3	Other anomalies of the larynx, trachea and bronchus (Must specify congenital tracheal stenosis, atresia of trachea, absence or agenesis of bronchus, trachea.)
748.4	Congenital cystic lung
748.5	Agenesis, hypoplasia, and dysplasia of the lung
748.61	Congenital bronchiectasis
750.15	Macroglossia
750.9	Uvula anomaly
759.89	Congenital malformation syndromes affecting multiple systems, not elsewhere classified (Beckwith Wiedmann Syndrome)