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N.L.: 01-0113
Index: Benefits
(Supercedes N.L.: 04-0509)

TO: ALL COUNTY CALIFORNIA CHILDREN SERVICES (CCS) PROGRAM
ADMINISTRATORS, MEDICAL CONSULTANTS, AND STATE
CHILDREN'S MEDICAL SERVICES (CMS) BRANCH STAFF

SUBJECT: PALIVIZUMAB (SYNAGIS™)

I. PURPOSE

The purpose of this numbered letter, which supercedes N.L.:04-0509, is to update CCS policy regarding the authorization of Palivizumab in conformance with the recommendations for immunoprophylaxis of Respiratory Syncytial Virus (RSV), as published in the American Academy of Pediatrics (AAP) 2012 Red Book. Large portions of the following sections are drawn from the latter; used with permission of the American Academy of Pediatrics. *Red Book: 2012 Report of the Committee on Infectious Diseases*. Pickering LK, ed. 29th ed. Elk Grove Village, IL.

II. BACKGROUND

Palivizumab (trade name Synagis) is a humanized monoclonal antibody produced by recombinant DNA technology licensed by the Federal Drug Administration (FDA) and indicated for the prevention of serious lower respiratory tract disease caused by RSV in pediatric patients at high risk of RSV disease.

In the temperate climates of North America, peak RSV activity typically occurs between November and March. The inevitability of the RSV season is predictable, but the severity of the season, the time of onset, the peak of activity, and the end of the season cannot be predicted precisely. Substantial variation in timing of community outbreaks of RSV disease from year to year exists in the same community 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. In recent years, the national median duration of the RSV season has been 19 weeks or less. Results from clinical trials indicate that palivizumab through serum concentrations more than 30 days after the fifth dose will be well above the protective concentration for most infants. Five monthly doses of palivizumab will provide more than 20 weeks of

protective serum antibody concentration. In the continental United States, a total of five monthly doses for infants and young children with congenital heart disease, CLD, or preterm birth before 32 weeks' gestation (31 weeks, 6 days and younger) will provide an optimal balance of benefit and cost, ***even with variation in season onset and end.***

For infants who qualify for five doses, initiation of immunoprophylaxis in November and continuation for a total of five monthly doses will provide protection into April. If prophylaxis is initiated in October, the fifth and final dose should be administered in February.

III. POLICY

- A. Palivizumab, up to five doses per RSV season, is a benefit for CCS clients, regardless of the eligible medical condition, who meet the following criteria:
1. **Infants with Chronic Lung Disease (CLD).** Infants and children ***younger than 24 months of age*** who receive supplemental oxygen, bronchodilator, diuretic or chronic corticosteroid therapy for CLD within six months before the start of the RSV season. These infants and young children should receive a maximum of five doses. Patients with the most severe CLD who continue to require medical therapy may benefit from prophylaxis during a second RSV season.
 2. **Infants born before 32 weeks' gestation (at or before 31 weeks, 6 days of gestation) (see Table 2).** These infants may benefit from RSV prophylaxis even if they do not have CLD. Infants born at or before 28 weeks, 6 days' gestation may benefit from prophylaxis during the RSV season, whenever that occurs during the first 12 months of life. Infants born at 29 weeks, 0 days through 31 weeks, 6 days of gestation 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 should not stop when the infant reaches either 6 months or 12 months of age. A maximum of five monthly doses is recommended for infants in this category.
 3. **Infants born at 32 to less than 35 weeks' gestation (defined as 32 weeks, 0 days through 34 weeks, 6 days of gestation).** Palivizumab prophylaxis should be limited to infants younger than three months of age at the start of the RSV season or who are born during the RSV season and 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 are present:
 - The infant attends child care, defined as a home or facility where care is provided for any number of infants or young toddlers; or

- One or more older siblings younger than five years of age or other children younger than five years of age lives permanently in the same household. Multiple births younger than one year of age do not qualify as fulfilling this risk factor.

Prophylaxis may be considered for infants born at 32 through less than 35 weeks' gestation (defined as 32 weeks, 0 days through 34 weeks, 6 days of gestation) who are born less than three months before the onset of 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 three months of age and should receive a maximum of three monthly doses; many will receive only 1 or 2 doses before they reach three 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 three months of age for patients in this category.***

4. **Infants with congenital abnormalities of the airway or neuromuscular disease.** Immunoprophylaxis may be considered for infants who have either congenital abnormalities of the airway or a neuromuscular condition that compromises handling of respiratory secretions. Infants and young children in this category should receive a maximum of five doses of palivizumab ***during the first year of life.***
5. **Infants and children with Congenital Heart Disease (CHD).** 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 still require prophylaxis, a postoperative dose of palivizumab (15 mg/kg) should be considered as soon as the patient is medically stable.

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

6. **Immunocompromised children.** Infants and young children with severe immunodeficiencies (eg, severe combined immunodeficiency or advanced acquired immunodeficiency syndrome) may benefit from prophylaxis. Refer to Section IV for authorization requirements.

Special situations.

- If an infant or child who is receiving palivizumab immunoprophylaxis experiences a breakthrough RSV infection, monthly prophylaxis should continue until a maximum of 3 doses have been administered to infants in the 32 weeks, 0 days' through 34 weeks, 6 days' gestation 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 high-risk infants 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 co-circulates in a community.
 - 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. CCS considers "promptly" to mean within 48 hours.
 - 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.
- B. The following groups of infants are **NOT** at increased risk of RSV and generally should not receive immunoprophylaxis:
1. 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)
 2. Infants with lesions adequately corrected by surgery, unless they continue to require medication for congestive heart failure
 3. Infants with mild cardiomyopathy who are not receiving medical therapy for the condition
- C. **Patients with cystic fibrosis.** Routine prophylaxis in patients with cystic fibrosis is **NOT** indicated.

Table 1

Maximum Number of Monthly Doses of Palivizumab for Respiratory Syncytial Virus Prophylaxis

Infants Eligible for a Maximum of 5 Doses

- Infants younger than 24 months of age with chronic lung disease and requiring medical therapy
- Infants younger than 24 months of age and requiring medical therapy for congenital heart disease
- Preterm infants born at or before 31 weeks, 6 days of gestation
- Certain infants with neuromuscular disease or congenital abnormalities of the airways

Infants Eligible for a Maximum of 3 Doses

- Preterm infants with gestational age of 32 weeks, 0 days to 34 weeks, 6 days with at least 1 risk factor and born 3 months before or during RSV season.

Table 2

Maximum Number of Palivizumab Doses for RSV Prophylaxis of Preterm Infants Without Chronic Lung Disease, on the Basis of Birth Date, Gestational Age, and Presence of Risk Factors

Maximum No. of Doses for Season Beginning November 1			
Month of Birth	≤28 Weeks, 6 Days of Gestation and <12 Months of Age at Start of Season	29 Weeks, 0 Days Through 31 Weeks, 6 Days of Gestation and <6 Months of Age at Start of Season	32 Weeks, 0 Days Through 34 Weeks, 6 Days of Gestation and With Risk Factor^a
Nov 1–Mar 31 of previous RSV season	5 ^b	0 ^c	0 ^d
April	5	0 ^c	0 ^d
May	5	5	0 ^d
June	5	5	0 ^d
July	5	5	0 ^d
August	5	5	1 ^e
September	5	5	2 ^e
October	5	5	3 ^e
November	5	5	3 ^e
December	4	4	3 ^e
January	3	3	3 ^e
February	2	2	2 ^e
March	1	1	1 ^e

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

^a Risk factors: (1) infant attends child care; or (2) infant has sibling younger than 5 years of age.

^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 of age at 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 they are 90 days of age.

IV. POLICY IMPLEMENTATION

Authorizations:

- A. Palivizumab requires separate authorization for outpatient administration. Palivizumab injections are administered monthly.
- Except as noted immediately below, the request for service shall be from the CCS authorized pediatric subspecialist or CCS approved SCC; or the request shall be from a CCS approved pediatrician authorized in conjunction with a CCS approved pediatric subspecialist or CCS approved SCC.
 - For qualifying patients with CHD, the request for service should come from a CCS- approved: Cardiac Special Care Center (SCC); cardiologist from a CCS-approved Cardiac SCC; or a CCS-approved pediatrician authorized in conjunction with such a Cardiac SCC or cardiologist, in which case the cardiologist must explicitly indicate medical necessity.
 - For qualifying patients with severe immunodeficiencies, the request for service should come from a CCS approved- : Infectious Disease and Immunologic Disorder SCC; Transplant SCC; Hematology/Oncology SCC; or CCS-approved pediatrician authorized in conjunction with one of these SCCs, in which case the approved SCC must explicitly indicate medical necessity.
- B. Palivizumab does not need a separate authorization for inpatient administration.
- C. Palivizumab is a Medi-Cal benefit. Please refer to "This Computes!" for the current method of authorizing Palivizumab.
- D. *Expedite Palivizumab authorizations to help ensure prompt initiation of protection from RSV for the infant/child and to prevent a lapse in protection, especially for the infant who will frequently receive the first injection in the hospital prior to discharge.*

If you have any questions regarding this numbered letter, please contact your state regional office medical consultant.

Original Signed by Robert J. Dimand

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