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

**Release Date**
- December 2009

**Guideline Developer**

**INTENDED AUDIENCE**
- Users
- Care Setting

**TARGET POPULATION**
- **Inclusion Criterion**
  - Pediatric patients who are at increased risk of severe disease
- **Exclusion Criterion**

**KNOWLEDGE COMPONENTS**

**DEFINITIONS**

**RECOMMENDATION**: * Criteria 1. Infants with CLD (Page 4, Column 1, Paragraph 3)

<table>
<thead>
<tr>
<th>Conditional: 1.1 Infants with CLD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Decision Variable:</strong> Chronological Age</td>
</tr>
<tr>
<td><strong>Value:</strong> &lt; 24 months</td>
</tr>
<tr>
<td><strong>Description:</strong> within 6 months before Onset of RSV</td>
</tr>
<tr>
<td><strong>Decision Variable:</strong> CLD</td>
</tr>
<tr>
<td><strong>Value:</strong> TRUE</td>
</tr>
<tr>
<td><strong>Description:</strong> Dx of CLD</td>
</tr>
<tr>
<td><strong>Decision Variable:</strong> Receives medical therapy</td>
</tr>
<tr>
<td><strong>Value:</strong> TRUE</td>
</tr>
<tr>
<td><strong>Description:</strong> Receives medical therapy (supplemental oxygen, bronchodilator, diuretic or chronic corticosteroid therapy) for CLD</td>
</tr>
<tr>
<td><strong>Decision Variable:</strong> Onset of RSV</td>
</tr>
<tr>
<td><strong>Value:</strong> If Southeast Florida - July 1 If Location = North-central or southwest Florida - 9/15Else 11/1</td>
</tr>
<tr>
<td><strong>Description:</strong> Note, this refers to the supplemental treatment being performed within 6 months of RSV season</td>
</tr>
<tr>
<td><strong>Action:</strong> should receive a maximum of 5 doses.</td>
</tr>
<tr>
<td><strong>Reason:</strong> The primary benefit of immuno prophylaxis is a decrease in the rate of RSV associated hospitalization.</td>
</tr>
</tbody>
</table>
| **Evidence Quality:** Quality of Evidence = IThe efficacy of palivizumab has been evaluated in 2 multicenter, placebo controlled, randomized clinical trials, both of which used a
primary endpoint 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/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. 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 < 0.001]).

**Recommendation Strength:** Strength of Recommendation = A

**Logic:** If (Chronological Age < 24 months) AND (CLD = TRUE) AND (Receives medical therapy = TRUE) AND (Onset of RSV <= 6 months) Then May benefit from prophylaxis Receive a maximum of 5 doses

**Cost:** 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. 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.

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).

**Action:** may benefit from prophylaxis during a second RSV season.

**Action:** Individual patients may benefit from decisions made in consultation with neonatologists, pediatric intensivists, pulmonologists, or infectious disease specialists (AI).

**Reason:** The primary benefit of immuno prophylaxis is a decrease in the rate of RSV associated hospitalization. Patients with the most severe CLD who continue to require medical therapy may benefit from prophylaxis during a second RSV season.

**Evidence Quality:** Quality of Evidence = III (Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.)

"Data are limited regarding the effectiveness of palivizumab during the second year of life."

**Recommendation Strength:** Strength = C

**Logic:** If Conditional 1.1 = TRUE AND Received Synagis Prior Year = TRUE AND Severe CLD Then May benefit from prophylaxis during a second RSV season. Individual patients may benefit from decisions made in consultation with neonatologists, pediatric intensivists, pulmonologists, or infectious disease specialists (AI).

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<table>
<thead>
<tr>
<th>RECOMMENDATION:</th>
<th>* Criteria 2. Infants Gestational Age &lt; 32 weeks (Page 4, Column 2, Paragraph 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conditional:</td>
<td>2.1 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.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Decision Variable:</th>
<th>Gestational Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value:</td>
<td>&lt;= 28 Weeks</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Decision Variable:</th>
<th>Chronological Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value:</td>
<td>&lt; 12 Months</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Decision Variable:</th>
<th>Onset of RSV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value:</td>
<td>TRUE</td>
</tr>
</tbody>
</table>

**Action:** May benefit from prophylaxis

**Action:** Receive maximum of 5 doses

**Action:** Receive all 5 doses

**Logic:** If (Gestational Age <= 28 Weeks) AND (Chronological Age < 1 year) AND (Onset of RSV) Then May benefit from prophylaxis Receive maximum of 5 doses Receive all 5 doses

<table>
<thead>
<tr>
<th>Conditional:</th>
<th>2.2 Infants born at 29 to 32 weeks’ gestation (31 weeks 6 days) may benefit most from prophylaxis up to 6 months of</th>
</tr>
</thead>
</table>
**Decision Variable:** Gestational Age  
**Value:** $\geq 29$ weeks AND $\leq 32$ weeks

**Decision Variable:** Chronological Age  
**Value:** $\leq 6$ months

**Decision Variable:** Onset of RSV  
**Value:**  
- If Location = Southeast Florida Then July
- ElseIf Location = North-central or southwest Florida Then September 15
- Else Then November 1

**Decision Variable:** CLD  
**Action:** May benefit from prophylaxis  
**Action:** Receive maximum of 5 doses  
**Action:** Receive all 5 doses

**Logic:**  
If (Gestational Age $\geq 29$ weeks AND Gestational Age $\leq 31$ weeks 6 days) AND (Chronological Age $\leq 6$ months) AND (Onset of RSV =TRUE) Then May benefit from prophylaxis Receive maximum of 5 doses Receive all 5 doses

**RECOMMENDATION:** * Criteria 3. Infants Gestational Age $> 32$ & $< 35$ weeks (Page 4, Column 2, Paragraph 3)

**Conditional:**  
3.1 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.

**Decision Variable:** Gestational Age  
**Value:** $\geq 32$ weeks and $\leq 35$ weeks

**Decision Variable:** Chronological Age  
**Value:** $< 90$ days

**Decision Variable:** Attends Childcare  
**Value:** TRUE  
**Description:** 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;

**Decision Variable:** Other children $< 5$ years in household.  
**Value:** TRUE  
**Description:** 1 or more siblings or other children younger than 5 years live permanently in the same household.

**Decision Variable:** Onset of RSV Season  
**Value:**  
- If Location = Southeast Florida Then July
- ElseIf Location = North-central or southwest Florida Then September 15
- Else Then November 1

**Action:** Prophylaxis may be considered

**Action:** Receive prophylaxis only until they reach 3 months
of age

**Action:** Receive a maximum of 3 monthly doses;

**Reason:** 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:

**Logic:** If (Gestational Age >= 32 weeks AND Gestational Age <= 35 weeks) AND (Chronological Age <= 90 Days) AND (Onset of RSV Season) AND (Attends Childcare = TRUE OR Other children < 5 years in household = TRUE) Then Prophylaxis may be considered Receive prophylaxis only until they reach 3 months of age Receive a maximum of 3 monthly doses

**RECOMMENDATION:** * Criteria 4. Infants with congenital abnormalities of the airway or neuromuscular disease.

**Conditional:** 4.1 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.

**Decision Variable:** Chronological Age  
**Value:** < 1 Year  
**Decision Variable:** Congenital abnormalities of the airway  
**Value:** TRUE  
**Description:** significant congenital abnormalities of the airway  
**Decision Variable:** Neuromuscular condition  
**Action:** Immunoprophylaxis may be considered  
**Action:** Receive a maximum of 5 doses of palivizumab during the first year of life  
**Logic:** If Chronological Age < 1 Year AND (Congenital abnormalities of the airway = TRUE) OR Neuromuscular condition = TRUE) Then Immunoprophylaxis may be considered Receive a maximum of 5 doses during the first year of life

**RECOMMENDATION:** * Criteria 5. Infants and children with CHD:

**Conditional:** 5.1 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.

**Decision Variable:** Chronological Age  
**Value:** <= 24 Months  
**Decision Variable:** CHD  
**Value:** TRUE  
**Description:** hemodynamically significant cyanotic or
acyanotic CHD

**Decision Variable:** CHD Medication  
**Value:** TRUE  
**Description:** receiving medication to control congestive heart failure

**Decision Variable:** Pulmonary hypertension  
**Value:** TRUE  
**Description:** infants with moderate-to-severe pulmonary hypertension;

**Decision Variable:** Cyanotic heart disease  
**Value:** TRUE  
**Action:** may benefit from palivizumab prophylaxis  
**Logic:** If (Chronological Age <= 24 months) AND (CHD = TRUE) AND (CHD Medication = TRUE OR Pulmonary hypertension = TRUE OR Cyanotic heart disease = TRUE)  
Then may benefit from palivizumab prophylaxis

**Conditional:** 5.2 After surgical procedures that use cardiopulmonary bypass

**Decision Variable:** Conditional 5.1  
**Value:** TRUE  

**Decision Variable:** Surgical procedure that use cardiopulmonary bypass  
**Value:** TRUE  
**Action:** a postoperative dose of palivizumab (15 mg/kg) should be administered as soon as the patient is medically stable (AI).  
**Reason:** a mean decrease in palivizumab serum concentration of 58% was observed after surgical procedures that use cardiopulmonary bypass  
**Logic:** If Conditional 5.1 = TRUE AND Surgical procedure that use cardiopulmonary bypass Then A postoperative dose of palivizumab (15 mg/kg) should be administered as soon as the patient is medically stable (AI).

**Conditional:** 5.3 Infants with CHD not at increased risk

**Decision Variable:** 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);  
**Decision Variable:** with lesions adequately corrected by surgery, unless they continue to require medication for congestive heart failure;  
**Decision Variable:** with mild cardiomyopathy who are not receiving medical therapy for the condition.  
**Action:** are not at increased risk of RSV and generally should not receive immunoprophylaxis  
**Logic:** If with hemodynamically insignificant heart disease
(eg, secundum atrial septal defect, small ventricular septal defect, pulmonicstenosis, uncomplicated aortic stenosis, mild coarctation of the aorta, and patent ductus arteriosus); OR with lesions adequately corrected by surgery, unless they continue to require medication for congestive heart failure OR with mild cardiomyopathy who are not receiving medical therapy for the condition. Then are not at increased risk of RSV and generally should not receive immunoprophylaxis

### RECOMMENDATION: * Criteria 6. Immunocompromised children

<table>
<thead>
<tr>
<th>Conditional:</th>
<th>6.1 Immunocompromised</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Decision Variable:</strong></td>
<td>Severe immunodeficiency</td>
</tr>
<tr>
<td><strong>Value:</strong></td>
<td>TRUE</td>
</tr>
<tr>
<td><strong>Description:</strong></td>
<td>severe combined immunodeficiency or advanced AIDS</td>
</tr>
<tr>
<td><strong>Action:</strong></td>
<td>May benefit from prophylaxis</td>
</tr>
</tbody>
</table>

**Evidence Quality:** 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).

**Logic:** If Severe immunodeficiency Then May benefit from prophylaxis

### RECOMMENDATION: * Criteria 7. Patients with cystic fibrosis

<table>
<thead>
<tr>
<th>Imperative:</th>
<th>7.1 A recommendation for routine prophylaxis in patients with cystic fibrosis cannot be made</th>
</tr>
</thead>
</table>


### RECOMMENDATION: * Criteria 8. Special situations

<table>
<thead>
<tr>
<th>Conditional:</th>
<th>8.1) Breakthrough RSV infection</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Decision Variable:</strong></td>
<td>Qualifies for prophylaxis</td>
</tr>
<tr>
<td><strong>Decision Variable:</strong></td>
<td>is receiving palivizumab immuno prophylaxis</td>
</tr>
<tr>
<td><strong>Decision Variable:</strong></td>
<td>Breakthrough RSV infection</td>
</tr>
<tr>
<td><strong>Action:</strong></td>
<td>Continue until a maximum number of doses have been administered</td>
</tr>
<tr>
<td><strong>Action:</strong></td>
<td>3 doses have been administered to infants in the 32 weeks’ 0 days’ through 34 weeks’ 6 days’ gestational-age group o</td>
</tr>
<tr>
<td><strong>Action:</strong></td>
<td>Maximum of 5 doses have been administered to</td>
</tr>
</tbody>
</table>
infants with CHD, CLD, or preterm birth before 32 weeks’ gestation.

**Reason:** 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).

**Logic:** If Is receiving palivizumab immuno prophylaxis = TRUE AND Breakthrough RSV infection = TRUE Then Continue until a maximum number of doses have been administered 3 doses have been administered to infants in the 32 weeks’ 0 days’ through 34 weeks’ 6 days’ gestational-age group Maximum of 5 doses have been administered to infants with CHD, CLD, or preterm birth before 32 weeks’ gestation.

### Conditional: 8.2) Hospitalized infants who qualify for prophylaxis during the RSV season

| **Decision Variable:** Hospitalized | **Value:** If Location = Southeast FloridaThen July ElseIf Location = North-central or southwest FloridaThen September 15ElseThen November 1 |
| **Decision Variable:** Onset of RSV | **Action:** receive the first dose of palivizumab 48 to 72 hours before discharge or promptly after discharge(CIII). |
| **Logic:** If Conditional 1.1 - 5.3 = TRUE AND Hospitalized = TRUE AND Onset of RSV = TRUE Then receive the first dose of palivizumab 48 to 72 hours before discharge or promptly after discharge(CIII). |

### Conditional: 8.3) Hospitalized during course

| **Decision Variable:** is receiving palivizumab immuno prophylaxis | **Decision Variable:** hospitalized |
| **Decision Variable:** date when the next monthly dose is due should receive that dose as scheduled w | **Action:** receive that dose as scheduled while they remain in the hospital (AI). |

### Imperative: 8.4) Infection control

**Directive:** 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. 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).

**Imperative:** 8.5 Palivizumab does not interfere with response to vaccines.

**ALGORITHM:**