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)

Conditional: 1.1 Infants with CLD

Decision Variable: Chronological Age
Value: < 24 months
Description: within 6 months before Onset of RSV

Decision Variable: CLD
Value: TRUE
Description: Dx of CLD

Decision Variable: Receives medical therapy
Value: TRUE
Description: Receives medical therapy (supplemental oxygen, bronchodilator, diuretic or chronic corticosteroid therapy) for CLD

Decision Variable: Onset of RSV
Value: If Southeast Florida - July 1 If Location = North-central orsouthwest Florida - 9/15Else 11/1
Description: Note, this refers to the supplemental treatment being performed within 6 months of RSV season

Action: should receive a maximum of 5 doses.
Reason: The primary benefit of immuno prophylaxis is a decrease in the rate of RSV associated hospitalization.
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 diureticorcorticosteroidtherapywithin 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 Prophy4 laxis 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]).
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 prophylaxisReceive a maximum of 5 doses
Cost: Economic 7 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 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
Reference: 4. The IMpact-RSV Study Group. Palivizumab, a humanized respiratory syncytial virus monoclonal antibody, reduces hospitalization from respiratory syncytial virus infection in high risk infants.Pediatrics.1998;102(3):531–537

Conditional: 1.2 Severe CLD

Decision Variable: Conditional 1.1
Value: TRUE
Description: Infants with CLD

Decision Variable: Received Synagis Prior Year
Value: TRUE
Description: If received prophylaxis prior RSV season

Decision Variable: Severe CLD
Description: with the most severe CLD continue to require medical therapyPatients with the most severe CLD who continue to require medical therapy may benefit from prophylaxis during a second RSVseason. 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).

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).

RECOMMENDATION: * Criteria 2. Infants Gestational Age < 32 weeks (Page 4, Column 2, Paragraph 2)

Conditional: 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.

Decision Variable: Gestational Age

Value: <= 28 Weeks

Decision Variable: Chronological Age

Value: < 12 Months

Decision Variable: Onset of RSV

Value: TRUE

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

Conditional: 2.2 Infants born at 29 to 32 weeks' gestation (31 weeks 6 days) may benefit most from prophylaxis up to 6 months of

	age.
	Decision Variable: Gestational Age **Value:** >= 29 weeks AND <= 32 weeks **Decision Variable:** Chronologial Age **Value:** <= 6 months **Decision Variable:** Onset of RSV **Value:** If Location = Southeast FloridaThen July 1ElseIf Location = North-central orsouthwest FloridaThen September 15ElseThen 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 >= 29 weeks AND Gestational Age <= 31 weeks 6 days) AND (Chronologial Age < 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:** >= 32 weeks and <= 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 FloridaThen July 1ElseIf Location = North-central orsouthwest FloridaThen September 15ElseThen 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 thatRSV infection is more likely to oc-cur and more likely to lead to hos-pitalization for infants in thisgestational-age group when atleast 1 of the following 2 risk fac-tors 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.5
	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, pulmonicstenosis,uncomplicatedaortic stenosis, mild coarctation of the aorta,andpatentductusarteriosus); **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,uncomplicatedaortic stenosis, mild coarctation of the aorta,andpatentductusarteriosus); 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

Conditional: 6.1 Immunocompromised

Decision Variable: Severe immunodeficiency

Value: TRUE

Description: severe combined immunodeficiency or advanced AIDS

Action: May benefit from prophylaxis

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

Imperative: 7.1 A recommendation for routine prophylaxis in patients with cystic fibrosis cannot be made

Evidence Quality: insufficient data exist to determine the effectiveness of palivizumab use in this patient population.31. Giusti R. North American Synagis Prophylaxis survey. Pediatr Pulmonol. 2009;44(1): 96–98

RECOMMENDATION: * Criteria 8. Special situations

Conditional: 8.1) Breakthrough RSV infection

Decision Variable: Qualifes for prophylaxis

Decision Variable: is receiving palivizumab immuno prophylaxis

Decision Variable: Breakthrough RSV infection

Action: Continue until a maximum number of doses have been administered

Action: 3 doses have been administered to infants in the 32 weeks' 0 days' through 34 weeks' 6 days' gestational-age group o

Action: Maximum of 5 doses have been administered to

	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 s
	Decision Variable: Hospitalized **Decision Variable:** Onset of RSV **Value:** If Location = Southeast FloridaThen July 1ElseIf Location = North-central orsouthwest FloridaThen September 15ElseThen November 1 **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:** eceive that dose as scheduled while they remain in the hospital (AI).
Imperative:	8.4) Infection control
	Directive: RSVisknowntobetransmittedin the hospital setting and to cause serious disease in infants at high risk. Among hospitalized infants, the major means of reducing RSV transmissionisstrictobservance of infection-control practices, including prompt initiation of precautions for RSV-infected infants.32 If an RSV outbreak occurs .32 If in a high-risk unit (eg, PICU or NICU or stem cell transplantation unit), primary emphasis should be placed on proper infectioncontrolpractices,especiallyhand hygiene. No data exist to support palivizumab use in controlling outbreaks of

	health care–associateddisease,andpalivizumabuse is not recommended for this purpose (CIII).
Imperative:	8.5 Palivizumab does not interfere with response to vaccines.

ALGORITHM: