TEXAS CHILDREN'S HOSPITAL
EVIDENCE-BASED OUTCOMES CENTER
Palivizumab (Synagis) Prophylaxis in Hospitalized Patients
Evidence Summary

Inclusion Criteria
- Infants born before 29 weeks of gestation
- Infants born before 32 weeks, 0 days of gestation with chronic lung disease (CLD) defined as > 21% oxygen for at least 28 days after birth
- Infants with hemodynamically significant heart disease, specifically:
    - Infants with cyanotic heart defect with consultation of a cardiologist
    - Infants with acyanotic heart disease who are receiving medication to control congestive heart failure and will require future cardiac surgical procedures
    - Infants with moderate-to-severe pulmonary hypertension

Exclusion Criteria
- Not recommended in the 2nd year of life except for children who require at least 28 days of supplemental oxygen after birth and who continue to require medical intervention (supplemental oxygen, chronic corticosteroid or diuretic therapy).

Background

In the United States, respiratory syncytial virus (RSV) is the leading cause of bronchiolitis in infants and young children. [(1)] It accounts for approximately 125,000 hospitalizations and 250 infant deaths every year in the United States. Typically, most children contract RSV at least once by the age of 2 and are managed effectively with supportive care. However, infants born prematurely (defined as <37 weeks gestational age [wGA] and those with certain underlying medical conditions such as chronic lung disease (CLS) or congenital heart disease are at increased risk for severe, and possibly life-threatening RSV disease (see inclusion criteria above). [(2)] Palivizumab (Synagis®) is a US Food and Drug Administration (FDA) approved monoclonal antibody which is recommended by the American Academy of Pediatrics (AAP) as immunoprophylaxis in high-risk infants and young children. Palivizumab has demonstrated efficacy in reducing hospitalizations and preventing serious lower respiratory infections in this population.

Critically Analyze the Evidence

The **GRADE criteria** were used to evaluate the quality of evidence presented in research articles reviewed during the development of this guideline. The table below defines how the quality of evidence is rated and how a strong versus a weak recommendation is established.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
WEAK	Desirable effects closely balanced with undesirable effects
Quality	**Type of Evidence**
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
Moderate	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
Low	Evidence for at least 1 critical outcome from observational studies, from RCTs with serious flaws or indirect evidence
Very Low	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence

PICO Question 1: In hospitalized infants and young children at increased risk for community-acquired respiratory syncytial virus (RSV), does palivizumab (Synagis) prophylaxis administered 48 to 72 hours before discharge or promptly after discharge decrease the risk of community-acquired RSV infections (i.e., length of stay, morbidity, and mortality)?

Recommendation(s): Strong recommendation with **low quality evidence** to administer palivizumab prophylaxis for community-acquired RSV, 48 to 72 hours before discharge or promptly after discharge, to: [(5-17)]
- In the first year of life for infants born before 29 weeks, 0 days' gestation
- For preterm infants with CLD of prematurity, defined as birth at <32 weeks, 0 days' gestation and a requirement for >21% oxygen for at least 28 days after birth
- Infants with hemodynamically significant heart disease
    - Infants with cyanotic heart defect with consultation of a cardiologist

  - Infants with acyanotic heart disease who are receiving medication to control congestive heart failure and will require future cardiac surgical procedures
  - Infants with moderate-to-severe pulmonary hypertension
- For children in the second year of life who required at least 28 days of supplemental oxygen after birth and who continue to require medical intervention (supplemental oxygen, chronic corticosteroid, or diuretic therapy.

Remarks: The first dose of palivizumab should be administered to the patient prior to discharge (within 48 to 72 hours) and the subsequent doses are administered outpatient. **Please consult the Pharmacy and Therapeutics Committee for a multidisciplinary decision to administer palivizumab to patients who do not meet the criteria of this recommendation.**

PICO Question 2: In hospitalized infants and young children, should Palivizumab prophylaxis be used in prevention of health-care associated RSV disease?

Recommendation(s): Strong recommendation with **low quality evidence** to not use Palivizumab prophylaxis for prevention of health care-associated RSV disease. [18-20]
Remarks: Current evidence not support the use of palivizumab prophylaxis for the prevention of healthcare associated RSV disease. **Please consult the Pharmacy and Therapeutics Committee for a multidisciplinary decision to administer palivizumab to patients who do not meet the criteria of recommendation #1.**

Critical Points of Evidence*

Evidence Supports

Administration of palivizumab (Synagis) prophylaxis for community-acquired RSV 48 to 72 hours before discharge or promptly after discharge: [5-17] – Strong recommendation, low quality evidence

- In the first year of life for infants born before 29 weeks, 0 days' gestation
- For preterm infants with CLD of prematurity, defined as birth at <32 weeks, 0 days' gestation and a requirement for >21% oxygen for at least 28 days after birth
- Infants with hemodynamically significant heart disease
  - Infants with cyanotic heart defect with consultation of a cardiologist
  - Infants with acyanotic heart disease who are receiving medication to control congestive heart failure and will require future cardiac surgical procedures
  - Infants with moderate-to-severe pulmonary hypertension
- For children in the second year of life who required at least 28 days of supplemental oxygen after birth and who continue to require medical intervention (supplemental oxygen, chronic corticosteroid, or diuretic therapy.

Evidence Against

- Administration of palivizumab (Synagis) prophylaxis for the prevention of health care-associated RSV disease.[18-20] – Strong recommendation, low quality evidence

Evidence Lacking/Inconclusive

- Additional populations may be considered for palivizumab (Synagis) prophylaxis given that medical services provide specific data/evidence to the Pharmacy and Therapeutics Committee documenting the benefit of this drug in their patient population. **Please consult the Pharmacy and Therapeutics Committee for a multidisciplinary decision to administer palivizumab to patients who do not meet the criteria.** Modifications will be made to the criteria based upon Pharmacy and Therapeutics Committee approval.

*NOTE: The references cited represent the entire body of evidence reviewed to make each recommendation.

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Clinical Standards Preparation

This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children's Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

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No relevant financial or intellectual conflicts to report.

Development Process

This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:

1. Review Preparation
   - PICO questions established
   - Evidence search confirmed with content experts
2. Review of Existing External Guidelines
   - Consensus document of antithrombotic therapy in the setting of electrophysiological procedures
   - PACES/HRS expert consensus statement on the use of catheter ablation in children and patients with congenital heart disease
   - Guidelines for the diagnosis, prevention and management of implantable cardiac electronic device infection
   - Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery

   Update on Cardiovascular Implantable Electronic Device Infections and Their Management
3. Literature Review of Relevant Evidence
   - Searched: Cochrane Collaboration, CINAHL, PubMed, PubMed Academic, Google Scholar
4. Critically Analyze the Evidence
   - Systematic reviews/meta-analyses, 2; randomized controlled trials, 1; observational studies, 12.
5. Summarize the Evidence
   - Materials used in the development of the clinical standard, literature appraisal, and any order sets are maintained in a Synagis Prophylaxis evidence-based review manual within EBOC.

Evaluating the Quality of the Evidence

Published clinical guidelines were evaluated for this review using the **AGREE II** criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline.

This clinical standard specifically summarizes the evidence *in support of* or *against* specific interventions and identifies where evidence is *lacking/inconclusive*. The following categories describe how research findings provide support for treatment interventions.

"Evidence Supports" provides evidence to support an intervention
"Evidence Against" provides evidence against an intervention.
"Evidence Lacking/Inconclusive" indicates there is insufficient evidence to support or refute an intervention and no conclusion can be drawn *from the evidence.*

The **GRADE** criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. The literature appraisal reflects the critical points of evidence.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
WEAK	Desirable effects closely balanced with undesirable effects
Quality	**Type of Evidence**
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
Moderate	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
Low	Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence
Very Low	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence

Recommendations

Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the post ablation and pacemaker implant management in children. When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

Approval Process

Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children's Hospital. Content Expert Teams are involved with every review and update.

Disclaimer

Practice recommendations are based upon the evidence available at the time the clinical standard was developed. Clinical standards (guidelines, summaries, or pathways) do not set out the standard of care and are not intended to be used to dictate a course of care. Each physician/practitioner must use his or her independent judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient's family, to make the ultimate judgment regarding care.

Version History

Date	Comments
Mar 2016	Originally completed
Jan 2020	Updated