



Louisiana

Immune Prophylaxis for Respiratory Syncytial Virus

Policy # 00177

Original Effective Date: 08/24/2005

Current Effective Date: 04/13/2020

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider monthly administration of immune prophylaxis for respiratory syncytial virus (RSV) with palivizumab (Synagis®)[‡] during respiratory syncytial virus (RSV) season in infants and children who meet guidelines from the American Academy of Pediatrics (AAP) to be **eligible for coverage**.**

Patient Selection Criteria

Administration of immune prophylaxis for respiratory syncytial virus (RSV) will be considered when the criteria are met for the respective category of "high risk" patient:

- 1. Infants born prematurely [WITHOUT chronic lung disease (CLD) OR WITHOUT hemodynamically significant cyanotic or acyanotic heart disease OR WITHOUT other listed "high risk" factors]:**
 - a. The infant is \leq 1 year of age at the start of the respiratory syncytial virus (RSV) season and was born before 29 weeks, 0 days' gestation (\leq 28 weeks, 6 days' gestation).
- 2. Children WITH chronic lung disease (CLD) (one of the below sets of criteria must be met):**
 - a. Infants \leq 1 year of age at the start of the respiratory syncytial virus (RSV) season:
 - i. The infant was born at $<$ 32 weeks, 0 days' gestation; AND
 - ii. The infant required $>$ 21% oxygen for at least 28 days after birth.OR
 - b. Children \leq 2 years of age at the start of the respiratory syncytial virus (RSV) season (second season dosing):

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- i. The child was born at < 32 weeks, 0 days' gestation; AND
- ii. The child required > 21% oxygen for at least 28 days after birth; AND
- iii. The child has required medical therapy (i.e., supplemental oxygen, diuretic therapy, or chronic corticosteroid therapy) during the 6 months before the start of the second respiratory syncytial virus (RSV) season.

3. Infants with congenital heart disease (CHD):

- a. The infant is ≤ 1 year of age at the start of the respiratory syncytial virus (RSV) season; AND
- b. The infant meets one of the following conditions:
 - i. The infant has hemodynamically significant cyanotic congenital heart disease (CHD); OR
 - ii. The infant has acyanotic heart disease AND is receiving medication to control congestive heart failure AND will require a cardiac surgical procedure; OR
 - iii. The infant has moderate to severe pulmonary hypertension; OR
 - iv. The infant has lesions that have been adequately corrected by surgery, but continues to require medication for congestive heart failure.

4. Children with cardiac transplant:

- a. The child is < 2 years of age at the start of the respiratory syncytial virus (RSV) season; AND
- b. The child has undergone or will undergo cardiac transplantation during the current respiratory syncytial virus (RSV) season.

5. Infants with a congenital anatomic pulmonary abnormality or neuromuscular disease:

- a. The infant is ≤ 1 year of age at the start of the respiratory syncytial virus (RSV) season; AND
- b. The infant's congenital anatomic pulmonary abnormality or neuromuscular disease impairs the ability to clear secretions from the upper airways.

6. Immunocompromised children:

- a. The child is younger than 24 months of age at the start of the respiratory syncytial virus (RSV) season;
AND

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- b. The child is/will be profoundly immunocompromised during the respiratory syncytial virus (RSV) season (e.g., chemotherapy or transplant).

Note: Children receiving approval for Synagis will be eligible for monthly dosing from the time of authorization until the end of the Blue Cross Blue Shield of Louisiana (BCBSLA) respiratory syncytial virus (RSV) season.

Note: Monthly prophylaxis should be discontinued in any child who experiences a breakthrough respiratory syncytial virus (RSV) hospitalization

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers immune prophylaxis for respiratory syncytial virus (RSV) in children that do NOT meet the requirements of the most current American Academy of Pediatrics (AAP) respiratory syncytial virus (RSV) Prophylaxis Guidelines to be **not medically necessary.****

Based on review of available data, the Company considers immune prophylaxis for respiratory syncytial virus (RSV) for any of the following (UNLESS OTHER “HIGH RISK” FACTORS ARE PRESENT and subsequent criteria in the patient selection criteria listed above are met) to be **not medically necessary****:

- Prevention of respiratory syncytial virus (RSV) in infants and children with hemodynamically insignificant heart disease (e.g., secundum atrial septal defect, small ventricular septal defect, pulmonic stenosis, mild coarctation of the aorta, and patent ductus arteriosus)
- Prevention of respiratory syncytial virus (RSV) in infants with mild cardiomyopathy who are not receiving medical therapy for the condition
- Prevention of respiratory syncytial virus (RSV) in patients with Cystic Fibrosis
- Prevention of respiratory syncytial virus (RSV) in patients with Down Syndrome.

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When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of Synagis for non-U.S. Food and Drug Administration (FDA) approved indications such as use in adults or treatment of respiratory syncytial virus (RSV) to be **investigational**.*

Background/Overview

RSV is the most common cause of lower respiratory infections in children. Immune prophylaxis against RSV is a prevention strategy to reduce the incidence of infection and its associated morbidity, including hospitalization, in high risk infants. RSV infections typically occur in the winter months, starting from late October to mid-January and ending from March to May. The BCBSLA RSV season is typically defined as occurring at the beginning of October and concluding at the end of March of the following year. Decisions for April coverage are made each year at the end of March based on RSV surveillance data. Considerable variation in the timing of community outbreaks is observed year to year. According to the Centers for Disease Control and Prevention (CDC), onset of the RSV season occurs when the median percentage of specimens testing positive for RSV is 10% higher over a 2-week period.

Synagis is a humanized monoclonal antibody that has neutralizing and fusion-inhibitory activity against RSV. Synagis is approved by the FDA for the prevention of serious lower respiratory tract disease caused by RSV in pediatric patients at high risk of RSV disease. Synagis is dosed at 15mg/kg per dose on a monthly basis. In the absence of a specific definition of “high risk” by the FDA, the AAP has been providing pediatricians and other health care providers with more precise guidance for determining who is at increased risk since Synagis was first licensed.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

In June 1998, the biologic drug palivizumab (Synagis; MedImmune, Gaithersburg, MA) was approved for marketing by FDA through a biologics license application (BLA) for use in the prevention of serious lower respiratory tract disease caused by RSV in pediatric patients at high risk

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of RSV disease. In 2004, FDA approved a liquid formulation of Synagis, supplied as a sterile solution ready for injection, thus providing improved convenience for administration. This formulation is used in the physician office or home setting. There are no therapeutic equivalents to this drug. FDA application number: (BLA) 103770.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Respiratory Syncytial Virus (Package Insert Data)

In the 1998 Impact-RSV Study Group, prophylaxis with palivizumab for preterm infants without CLD or children with CLD resulted in a 55% reduction in RSV hospital admission; 4.8% (48/1,002) in the palivizumab group and 10.6% (53/500) in the no prophylaxis group. Similar reductions in other measures of RSV severity in breakthrough infections were also reported. In a 2003 double-blind, placebo-controlled randomized trial of 1287 children with hemodynamically significant CHD, Feltes et al reported prophylaxis with palivizumab was associated with a 45% reduction in hospitalization rate for RSV among children with CHD. Hospitalization rates for RSV were 5.3% (34/639) in the palivizumab group and 9.7% (63/648) in the no prophylaxis group. The authors concluded that prophylaxis with palivizumab is clinically effective for reducing the risk of serious lower respiratory tract infection caused by RSV infection and requiring hospitalization in high-risk children.

American Academy of Pediatrics Guidelines

The AAP recently released new guidelines for the prophylaxis of RSV. The update included significant changes in the populations that are viewed as “high risk” for acquiring RSV. A few notable changes are the ages for premature populations and the change in second season dosing (except in a small population).

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Preterm Infants without Chronic Lung Disease

Data regarding the risk of RSV hospitalization for most preterm infants do not support a benefit from prophylaxis. In recent large cohort studies of moderately preterm infants, the majority of whom did not receive palivizumab, 2.5% to 4.9% required hospitalization for RSV infection during the RSV season indicating that more than 95% did not require hospitalization. The rate of hospitalization among infants ≥ 35 weeks' gestation (5.1/1000) was no different than the rate for term infants (5.3/1000). The hospitalization rate of infants ≥ 30 weeks to 35 weeks' gestation indicate only a slight increase in risk (less than twofold). Data concerning host or environmental risk factors for hospitalization in preterm infants without CLD or CHD are inconsistent, with the exception of age younger than 3 months at the start of the RSV season, which has been associated with an increased risk of hospitalization. The environment should be optimized for all infants, but especially preterm infants, to prevent RSV. Environmental optimization includes breast milk feeds, immunization of household contacts for influenza, practicing hand and cough hygiene, and avoiding tobacco exposure and large group childcare during the first winter season, wherever possible.

Preterm Infants with Chronic Lung Disease

Studies have documented that infants and young children with CLD have increased rates of RSV hospitalization. Results from the IMPact-RSV trial evaluating all preterm infants with CLD (n = 762 randomized preterm infants) demonstrated that the RSV hospitalization rate among placebo recipients was 12.8% and 7.9% among palivizumab recipients (P = .038).

Infants with Hemodynamically Significant Congenital Heart Disease

As mentioned above, the study looking at patients with CHD showed that hospitalization rates for RSV were 5.3% (34/639) in the palivizumab group and 9.7% (63/648) in the no prophylaxis group (p=0.003). There were 29 fewer RSV hospitalizations over the 4 year study in those that received palivizumab versus those that didn't receive prophylaxis. There appeared to be less benefit in cyanotic children than acyanotic children (23 fewer RSV hospitalizations/1000 palivizumab recipients vs. 68 fewer RSV hospitalizations/1000 palivizumab recipients). Other investigators describe the RSV hospitalization rate in those with hemodynamically significant CHD to be lower than the 9.7% reported in the earlier described study. A retrospective analysis of children younger than 3 years in the Tennessee Medicaid program revealed that the RSV hospitalization rate for children with CHD in the second year of life (18.2/1000) was less than half the hospitalization rate for low-risk infants in the first 5 months after birth (44.1/1000), a group for whom palivizumab

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prophylaxis is not recommended. Therefore, prophylaxis in the second year of life is not recommended for this population.

Children with Pulmonary Abnormalities or Neuromuscular Disorders

The risk of RSV hospitalization is not well defined in children with neuromuscular disorders that impair the ability to clear secretions from the upper airway. Studies have shown that those with neuromuscular disease that are hospitalized with RSV are likely older than other groups that are hospitalized and are more likely to have a pre-existing immunity to RSV.

Immunocompromised Children

The most current AAP guidelines (2014 update) state that, “Population-based data are not available on the incidence or severity of RSV disease among children who receive solid organ transplants (SOTs) or hematopoietic cell transplants (HCTs), children who receive chemotherapy, or children who are immunocompromised because of other conditions.” The guidelines also mention, “No data are available to suggest benefit from immunoprophylaxis among immunocompromised patients, and practices vary nationwide. Further research is required before definitive recommendations can be made for the use of palivizumab in this heterogeneous group of children. The AAP recommends that children younger than 24 months who will be profoundly immunocompromised during the RSV season may be considered for prophylaxis.

Other Indications

Cystic Fibrosis

A Cochrane review was published in 2010 and updated in 2013, assessing the use of palivizumab in children with cystic fibrosis. Based on a literature search through October 2012, 1 randomized comparative trial met the inclusion criteria of both reviews. In the study, 186 infants younger than 2 years with cystic fibrosis were randomly assigned to receive 5 monthly doses of palivizumab (n = 92) or placebo (n = 94). One member of each group was hospitalized for RSV within the 6-month follow-up period. The rate of adverse event noted in each group was relatively high, with serious adverse events not significantly different between the palivizumab and placebo groups (20.2% and 17.3%, respectively). The authors noted that it was not possible to draw conclusions on the tolerability and safety of RSV immune prophylaxis in cystic fibrosis. The single study reported similar adverse events but did not specify how adverse events were classified. No clinically meaningful outcome differences were noted at 6-month follow-up. The authors of the review called

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for additional randomized studies to establish both efficacy and safety of immune prophylaxis in children with cystic fibrosis.

Down Syndrome

Studies have shown that RSV prophylaxis would have a limited effect on RSV hospitalization for children with Down Syndrome without other risk factors for RSV.

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| 08/03/2005 | Medical Director review |
| 08/16/2005 | Medical Policy Committee review |
| 08/24/2005 | Managed Care Advisory Council approval |
| 12/20/2005 | Medical Policy Committee review. Clarification of post-operative dose following procedures requiring cardiopulmonary bypass to reflect the intent of policy to provide eligibility for children that would otherwise qualify for administration of immune prophylaxis for RSV. |
| 07/07/2006 | Format revision, including addition of FDA and or other governmental regulatory approval and rationale/source. Coverage eligibility unchanged. |
| 09/05/2007 | Medical Director review |
| 09/19/2007 | Medical Policy Committee approval. Coverage eligibility unchanged. |

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- 09/03/2009 Medical Policy Committee approval.
- 09/16/2009 Medical Policy Implementation Committee approval. Policy updated to adopt the American Academy of Pediatrics (AAP) 2009 Red Book Guidelines.
- 09/09/2010 Medical Policy Committee review
- 09/15/2010 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
- 09/01/2011 Medical Policy Committee review
- 09/14/2011 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
- 04/12/2012 Medical Policy Committee review
- 04/25/2012 Medical Policy Implementation Committee approval. Deleted the maximum of five doses from all of the criteria statements for immune prophylaxis for respiratory syncytial virus. Changed the criteria bullet to liberalize coverage regarding infants born at 28 weeks of gestation or earlier. These infants used to be eligible for coverage during their first respiratory syncytial virus season, but are now candidates for prophylaxis during the respiratory syncytial virus season, whenever that occurs during the first 12 months of life.
- 04/04/2013 Medical Policy Committee review
- 04/24/2013 Medical Policy Implementation Committee approval. Removed Respigam from the wording in the (When Services May Be Eligible for Coverage” section. On 1.b., clarified that it is referring to 1.a. On 1.g., deleted the wording regarding the max number of doses. Cleaned up the “When Services Are Considered Not Medically Necessary” and “When Services are Considered Investigational” sections.
- 04/03/2014 Medical Policy Committee review
- 04/23/2014 Medical Policy Implementation Committee approval. Added a few statements to clarify the administration of the policy. Clarified that multiple births do fulfill the requirement of another sibling in the household. Also added verbiage clarifying the dates of the BCBSLA RSV season and continuation of the season. Also clarified that patients receive the entire season for dosing unless specified in the patient selection criteria.
- 08/07/2014 Medical Policy Committee review
- 08/20/2014 Medical Policy Implementation Committee approval. Updated the policy to reflect changes in the 2014 American Academy of Pediatrics (AAP) Respiratory Syncytial Virus (RSV) Prophylaxis Guidelines.

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- 08/03/2015 Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
- 12/03/2015 Medical Policy Committee review
- 12/16/2015 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
- 10/01/2016 Coding update
- 12/01/2016 Medical Policy Committee review
- 12/21/2016 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
- 01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes
- 10/01/2017 Coding update
- 12/07/2017 Medical Policy Committee review
- 12/20/2017 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
- 12/06/2018 Medical Policy Committee review
- 12/19/2018 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
- 03/05/2020 Medical Policy Committee review
- 03/11/2020 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 03/2021

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2019 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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Louisiana

Immune Prophylaxis for Respiratory Syncytial Virus

Policy # 00177

Original Effective Date: 08/24/2005

Current Effective Date: 04/13/2020

Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	90378
HCPCS	S9562
ICD-10 Diagnosis	A18.84, I08.0-I08.9, I28.0-I28.9, I34.0-I34.9, I35.0-I35.9, I36.0-I36.9, I37.0-I37.9, I38-I39, I42.0-I42.943, I50.20-I50.23, I50.30-I50.33, I50.40-I50.43, I50.9, J41.0-J41.8, J42, J44.0-J44.9, M32.11, P07.20-P07.26, P07.30-P07.39, P29.3, Q20.0-Q20.9, Q21.0-Q21.9, Q22.0-Q22.9, Q23.0-Q23.9, Q24.0-Q24.9, Q25.0-Q25.6, Q25.71-Q25.79, Q25.8-Q25.9, Q26.0-Q26.9, Q27.0-Q27.9, Q28.0-Q28.9, Z36.0-Z36.9, Z41.8, Z99.81 Code added eff 1/1/2020: J44.0

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

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- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

****Medically Necessary (or “Medical Necessity”)** - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

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NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

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