Clinical Policy: Palivizumab (Synagis)

Reference Number: CP.PHAR.16
Effective Date: 08.01.09 Revision Log
Last Review Date: 05.20
Line of Business: Commercial, HIM, Medicaid

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Palivizumab (Synagis®) is a recombinant humanized mouse immunoglobulin monoclonal antibody which provides passive immunity against respiratory syncytial virus (RSV).

FDA Approved Indication(s)
Synagis is indicated for the prevention of serious lower respiratory tract disease caused by RSV in pediatric patients:

- With a history of premature birth (less than or equal to 35 weeks gestational age) who are 6 months of age or younger at the beginning of RSV season;
- With bronchopulmonary dysplasia (BPD) that required medical treatment within the previous 6 months and who are 24 months of age or younger at the beginning of RSV season;
- With hemodynamically significant congenital heart disease and who are 24 months of age or younger at the beginning of RSV season.

Limitation(s) of use: The safety and efficacy of Synagis have not been established for treatment of RSV disease.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Synagis is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Preterm Infant (must meet all)**:**

1. Diagnosis of preterm infant with gestational age < 29 weeks;
2. Age at onset of RSV season < 12 months;
3. Synagis prescription is written for RSV prophylaxis;
4. Member has not been hospitalized with RSV disease during the current RSV season;
5. Dose does not exceed 15 mg/kg once a month by intramuscular (IM) administration (*see Appendix E for dose rounding guidelines*).

Approval duration: up to 5 doses per RSV season

B. Chronic Lung Disease of Prematurity (must meet all):

1. Diagnosis of chronic lung disease (CLD) of prematurity (i.e., BPD) defined as gestational age < 32 weeks and a requirement for > 21% oxygen for ≥ 28 days after birth;

2. Age at onset of RSV season (a or b):
   a. Age < 12 months;
   b. Age ≥ 12 months to < 24 months and continues to require supplemental oxygen, chronic systemic corticosteroid therapy, or diuretic therapy within 6 months of the start of the RSV season;
3. Synagis prescription is written for RSV prophylaxis;
4. Member has not been hospitalized with RSV disease during the current RSV season;
5. Dose does not exceed 15 mg/kg once a month by IM administration (*see Appendix E for dose rounding guidelines*).

Approval duration: up to 5 doses per RSV season

C. Congenital Heart Disease (must meet all)**:**

1. Age and diagnosis at onset of RSV season (a or b):
   a. Age < 12 months and either (i or ii);
      i. Diagnosis of acyanotic heart disease and either (a or b):
         a) Receiving medication to control congestive heart failure AND will require a cardiac surgical procedure;
         b) Diagnosis of moderate to severe pulmonary hypertension;
      ii. Diagnosis of a cyanotic heart defect and RSV prophylaxis is recommended by a pediatric cardiologist;
   b. Age < 24 months and undergoing cardiac transplantation or cardio-pulmonary bypass during the current RSV season;
2. Synagis prescription is written for RSV prophylaxis;
3. Member has not been hospitalized with RSV disease during the current RSV season;
2. Dose does not exceed 15 mg/kg once a month by IM administration (*see Appendix E for dose rounding guidelines*).

Approval duration: up to 5 doses per RSV season *(6 doses if cardio-pulmonary bypass)*

D. Anatomic Pulmonary Abnormalities, Neuromuscular Disorders, Infants Profoundly Immunocompromised (must meet all)**:**

1. Age and diagnosis at onset of RSV season (a or b):
   a. Age < 12 months and diagnosis of an anatomic pulmonary abnormality or neuromuscular disorder that impairs the ability to clear secretions from the upper airway (e.g., due to ineffective cough);
   b. Age < 24 months and will be profoundly immunocompromised during the RSV season (e.g., due to solid organ or hematopoietic stem cell transplantation, chemotherapy, severe combined immunodeficiency, chronic granulomatous disease);
2. Synagis prescription is written for RSV prophylaxis;
3. Member has not been hospitalized with RSV disease during the current RSV season;
4. Dose does not exceed 15 mg/kg once a month by IM administration (*see Appendix E for dose rounding guidelines*).

Approval duration: up to 5 doses per RSV season

E. Cystic Fibrosis (must meet all)**:**
1. Diagnosis of cystic fibrosis and one of the following (a or b):
   a. Clinical evidence of nutritional compromise;
   b. Diagnosis of CLD of prematurity defined as gestational age < 32 weeks and requirement for > 21% oxygen for ≥ 28 days after birth;
2. Age at onset of RSV season (a or b):
   a. Age < 12 months;
   b. Age < 24 months and (i or ii):
      i. Manifestations of severe lung disease (e.g., previous hospitalization for pulmonary exacerbation in the first year of life or abnormalities on chest radiography or chest computed tomography that persist when stable);
      ii. Weight for length < 10th percentile;
3. Synagis prescription is written for RSV prophylaxis;
4. Member has not been hospitalized with RSV disease during the current RSV season;
5. Dose does not exceed 15 mg/kg once a month by IM administration (*see Appendix E for dose rounding guidelines*).

Approval duration: up to 5 doses per RSV season

F. Alaska Native and Other American Indian Infants (must meet all):
1. Medical director consultation is required for requests relating to Alaska native and other American Indian infants that fall outside the criteria outlined above;
2. Alaska native infants: Eligibility for prophylaxis may differ from the remainder of the U.S. on the basis of epidemiology of RSV in Alaska, particularly in remote regions where the burden of RSV disease is significantly greater than in the general U.S. population,
3. Other American Indian infants: Limited information is available concerning the burden of RSV disease among American Indian populations. However, special consideration may be prudent for Navajo and White Mountain Apache infants in the first year of life.
4. Synagis prescription is written for RSV prophylaxis;
5. Member has not been hospitalized with RSV disease during the current RSV season;
6. Dose does not exceed 15 mg/kg once a month by IM administration (*see Appendix E for dose rounding guidelines*).

Approval duration: up to 5 doses per RSV season

G. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Synagis prescription is written for RSV prophylaxis;

3. Member has not yet received 5 doses of Synagis in the current RSV season *(6 doses if cardio-pulmonary bypass);*
4. Member has not been hospitalized with RSV disease during the current RSV season;
5. If request is for a dose increase, new dose does not exceed 15 mg/kg once a month by intramuscular administration (*see Appendix E for dose rounding guidelines*).

Approval duration: up to 5 doses per RSV season *(6 doses if cardio-pulmonary bypass)*

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or up to 5 doses per RSV season (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BPD: bronchopulmonary dysplasia
CLD: chronic lung disease of prematurity
FDA: Food and Drug Administration
RSV: respiratory syncytial virus

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): previous significant hypersensitivity reaction to Synagis
- Boxed warning(s): none reported

Appendix D: RSV Seasonal Durations across the United States

The RSV season may commence as early as September and continue through May. In Florida, the RSV season may begin at any time throughout the year.

Appendix E: Dose Rounding Guidelines

Weight-based Dose Range	Vial Quantity Recommendation
≤ 52.49 mg	1 vial of 50 mg/0.5 mL
52.5 mg – 104.99 mg	1 vial of 100 mg/1 mL
105 mg – 157.49 mg	1 vial of 50 mg/0.5 mL and 1 vial of 100 mg/1 mL
157.5 mg – 209.99 mg	2 vials of 100 mg/1 mL

Weight-based Dose Range	Vial Quantity Recommendation
210 mg – 262.49 mg	1 vial of 50 mg/0.5 mL and 2 vials of 100 mg/1 mL
262.5 mg – 314.99 mg	3 vials of 100 mg/1 mL

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
RSV prophylaxis in pediatric patients	15 mg/kg IM once a month	15 mg/kg/month; up to 5 doses per RSV season (1 extra dose if cardio-pulmonary bypass)

VI. Product Availability

Single-dose vial: 50 mg/0.5 mL, 100 mg/1 mL

VII. References

1. Synagis Prescribing Information. Gaithersburg, MD: MedImmune, LLC; May 2017. Available at https://www.azpicentral.com/synagis/synagis.pdf#page=1. Accessed February 6, 2020.
2. Policy Statement: Updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection. American Academy of Pediatrics Committee on Infectious Diseases; American Academy of Pediatrics Bronchiolitis Guidelines Committee. *Pediatrics.* August 2014; 134(2): e415-20. doi: 10.1542/peds.2014-1665. Reaffirmed February 2019.
3. Technical Report: Updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection. American Academy of Pediatrics Committee on Infectious Diseases; American Academy of Pediatrics Bronchiolitis Guidelines Committee. *Pediatrics.* August 2014; 134(2): e620-38. doi: 10.1542/peds.2014-1666.
4. Errata: RSV Policy Statement: Updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection. American Academy of Pediatrics. *Pediatrics.* December 2014; 134(6): 1221.
5. Respiratory syncytial virus infection (RSV): Trends and surveillance. Centers for Disease Control and Prevention website. Content source: National Center for Immunization and Respiratory Diseases (NCIRD), Division of Viral Diseases. Available at http://www.cdc.gov/rsv/research/us-surveillance.html. Page last reviewed: June 26, 2018. Accessed February 6, 2020.
6. Robbie, G, Zhao, L, Mondick, J, et al. Population Pharmacokinetics of Palivizumab, a Humanized Anti-Respiratory Syncytial Virus Monoclonal Antibody in Adults and Children. Antimicrobial Agents and Chemotherapy. Sept 2012; 56(9): 4927-4936.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
References reviewed and updated Specialist Review	07.13	07.13
Converted authorization guideline to algorithms	08.13	10.13
Specialist Review	07.14	
Updated according to 2014 AAP Guidelines:	08.14	08.14

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Prophylaxis changed to <29 wks from <32 wks and high risk infants <35 wks and to only one season of prophylaxis for prematurity Defined CLD and changed recommendation to 5 doses for all indications Prophylaxis now to be discontinued if experience a breakthrough RSV hospitalization Infants with CHD now only allowed prophylaxis in first year of life and Ped Cardio needs consultation with cyanotic heart disease Prophylaxis for pulmonary abnormality or neuromuscular disease recommended for only 1 year, and clarity provided for pulmonary abnormality		
Omitted profoundly immunocompromised ≤ 24 months and children younger than 2 years who undergo cardiac transplantation during RSV season patient populations based on strength of guideline recommendation.	07.15	08.15
Updated algorithms and Appendix B for clarity	11.15	
Added "is Synagis prescribed for RSV prophylaxis" question to algorithm for clarity. No change in intent of criteria. Updated template and disclaimer language	01.16	
Policy converted to new template. Prophylaxis for cardiac transplantation and profoundly immunocompromised infants added to criteria.	07.16	08.16
Safety information removed (hypersensitivity). Doses added.	07.17	08.17
2Q 2018 annual review: no significant changes; policies combined for Commercial and Medicaid; HIM line of business added; references reviewed and updated.	02.13.18	05.18
2Q 2019 annual review: RSV seasonal patterns are updated in Appendix D per the CDC and state health departments to indicate a season onset as early as September extending to as late as May (Florida seasonal information is updated to indicate possible year-round onset).	02.19.18	05.19
Ad hoc change made to clarify preterm/gestational age requirement in Section I.A.: diagnosis of preterm birth is updated to indicate diagnosis of preterm infant; defined as gestational age < 29 weeks is updated to indicate with gestational age < 29 weeks.	12.12.19	
2Q 2020 annual review: added appendix E: dose rounding guidelines; added reference to appendix E within criteria; revised HIM-Medical Benefit to HIM line of business; references reviewed and updated.	03.05.20	05.20

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.