Clinical Policy: Palivizumab (Synagis)

Reference Number: ERX.SPA.124
Effective Date: 10.01.16
Last Review Date: 05.21
Line of Business: Commercial, Medicaid

Revision Log

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

Description
Palivizumab (Synagis®) is a recombinant humanized mouse immunoglobulin (IgG1) 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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. Request is for RSV prophylaxis;
4. Medical justification supports requests for RSV prophylaxis extending beyond the identified season duration for Florida or beyond September through May for the remainder of the U.S. (*see Appendix D*);*
   **Elevated interseasonal activity has been observed since March 2021, the CDC has indicated that at this time it is not possible to anticipate the likely spread, peak, or duration of activity with any certainty; requests for RSV prophylaxis outside of the typical season by region may be considered*
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 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. Request is for RSV prophylaxis;
4. Medical justification supports requests for RSV prophylaxis extending beyond the identified season duration for Florida or beyond September through May for the remainder of the U.S. (*see Appendix D*);*
   **Elevated interseasonal activity has been observed since March 2021, the CDC has indicated that at this time it is not possible to anticipate the likely spread, peak, or duration of activity with any certainty; requests for RSV prophylaxis outside of the typical season by region may be considered*
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

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;
3. Request is for RSV prophylaxis;
4. Medical justification supports requests for RSV prophylaxis extending beyond the identified season duration for Florida or beyond September through May for the remainder of the U.S. (*see Appendix D*);*
   **Elevated interseasonal activity has been observed since March 2021, the CDC has indicated that at this time it is not possible to anticipate the likely spread, peak, or duration of activity with any certainty; requests for RSV prophylaxis outside of the typical season by region may be considered*
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 *(6 doses if cardio-pulmonary bypass)*

D. Anatomic Pulmonary Abnormalities, Neuromuscular Disorders, and Infants Profoundly Immunocompromised (off-label) (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. Request is for RSV prophylaxis;
3. Medical justification supports requests for RSV prophylaxis extending beyond the identified season duration for Florida or beyond September through May for the remainder of the U.S. (*see Appendix D*);*
   **Elevated interseasonal activity has been observed since March 2021, the CDC has indicated that at this time it is not possible to anticipate the likely spread, peak, or duration of activity with any certainty; requests for RSV prophylaxis outside of the typical season by region may be considered*
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

E. Cystic Fibrosis (off-label) (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. Request is for RSV prophylaxis;
4. Medical justification supports requests for RSV prophylaxis extending beyond the identified season duration for Florida or beyond September through May for the remainder of the U.S. (*see Appendix D*);*
   **Elevated interseasonal activity has been observed since March 2021, the CDC has indicated that at this time it is not possible to anticipate the likely spread, peak, or duration of activity with any certainty; requests for RSV prophylaxis outside of the typical season by region may be considered*
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

F. Alaska Native and Other American Indian Infants (off-label) (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. Request is for RSV prophylaxis;
5. Medical justification supports requests for RSV prophylaxis extending beyond the identified season duration for Florida or beyond September through May for the remainder of the U.S. (*see Appendix D*);*
   **Elevated interseasonal activity has been observed since March 2021, the CDC has indicated that at this time it is not possible to anticipate the likely spread, peak, or duration of activity with any certainty; requests for RSV prophylaxis outside of the typical season by region may be considered*
6. Member has not been hospitalized with RSV disease during the current RSV season;
7. 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

G. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;

2. Request is for RSV prophylaxis;
3. Member will not reach 24 months of age at the start of RSV season;
4. Medical justification supports requests for RSV prophylaxis extending beyond the identified season duration for Florida or beyond September through May for the remainder of the U.S. (*see Appendix D*);*
   **Elevated interseasonal activity has been observed since March 2021, the CDC has indicated that at this time it is not possible to anticipate the likely spread, peak, or duration of activity with any certainty; requests for RSV prophylaxis outside of the typical season by region may be considered*
5. Member has not yet received 5 Synagis doses in the current RSV season *(6 doses if cardio-pulmonary bypass);*
6. Member has not been hospitalized with RSV disease during the current RSV season;
7. If request is for a dose increase, new 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)*

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 policy – ERX.PA.01 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 - Initiation and Termination of RSV Prophylaxis

- Historical 2014-2017 CDC data from the 10 U.S. Department of Health and Human Services (HHS) regions, with the exception of Florida, shows RSV seasons commencing as early as September in some regions and ending as late as May in others.[2-3]
- Because 5 monthly Synagis doses at 15 mg/kg/dose will provide more than 6 months of serum palivizumab concentrations above the threshold for protection for most infants, administration of more than 5 monthly doses is not recommended within the continental U.S. Children who qualify for Synagis prophylaxis should receive the first dose at the onset of the RSV season. For qualifying infants born during the RSV season, fewer than 5 Synagis doses will be needed to provide protection until the RSV season ends in their region. A small number of sporadic RSV hospitalizations will occur before or after the main season in many areas of the U.S., but the greatest benefit from prophylaxis is derived during peak season and not when the incidence of RSV hospitalization is low.[4-7]
- Data from the Florida Department of Health (http://www.floridahealth.gov/diseases-and-conditions/respiratory-syncytial-virus/) may be used to determine the appropriate timing of Synagis prophylaxis across Florida's regions where RSV seasons may begin at different times throughout the year. However, despite Florida's variable region-specific RSV seasons, a maximum of 5 monthly Synagis doses should be adequate.[4-7]
- The Centers for Disease Control and Prevention (CDC) is issuing this health advisory to notify clinicians and caregivers about increased interseasonal respiratory syncytial virus (RSV) activity across parts of the Southern United States. Compared with previous years, RSV activity remained relatively low from May 2020 to March 2021. However, since late March, CDC has

observed an increase in RSV detections reported to the National Respiratory and Enteric Virus Surveillance System (NREVSS). CDC noted increases in laboratory detections and in the percentages of positive detections for both antigen and PCR testing in parts of HHS Region 4 (Alabama, Florida, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, and Tennessee) and Region 6 (Arkansas, Louisiana, New Mexico, Oklahoma, and Texas). Due to limited testing outside of the typical RSV season, data are limited in some jurisdictions and may be incomplete for the most recent weeks. Since this elevated interseasonal activity is a deviation in the typical circulation patterns for RSV, at this time it is not possible to anticipate the likely spread, peak, or duration of activity with any certainty.

*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
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

**This is part of a dose rounding guideline on select drug classes as part of an initiative conducted on a larger scale with multiple references and prescriber feedback.*

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 (one extra dose if cardio-pulmonary bypass)

VI. Product Availability

Single-dose vials: 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 17, 2021.
2. 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: December 18, 2020. Accessed February 17, 2021.
3. Rose EB, Wheatley A, Langley G, Gerber S, Haynes A. Respiratory Syncytial Virus Seasonality — United States, 2014–2017. MMWR Morb Mortal Wkly Rep 2018;67:71–76. DOI: http://dx.doi.org/10.15585/mmwr.mm6702a4.
4. Red Book® 2018. Committee on Infectious Diseases; American Academy of Pediatrics; David W. Kimberlin, MD, FAAP; Michael T. Brady, MD, FAAP; Mary Anne Jackson, MD, FAAP; Sarah S. Long, MD, FAAP. Section 3: Respiratory Syncytial Virus. Available at https://redbook.solutions.aap.org/Book.aspx?bookid=2205. Accessed February 17, 2021.
5. 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. Available online at https://pediatrics.aappublications.org/content/134/2/415. full#sec-13.
6. 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.

7. 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.
8. 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.
9. CDC Health Alert Network: Increased Interseasonal Respiratory Syncytial Virus (RSV) Activity in Parts of the Southern United States. June 10, 2021. Available at: https://emergency.cdc.gov/han/2021/han00443.asp. Accessed July 6, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Doses added. References updated. Note: age limitation for CHD is maintained at < 12 months (as opposed to < 24 months) per AAP guidelines.	07.17	08.17
2Q 2018 annual review: CHD bypass and transplantation age delineated as < 24 months per AAP guidelines; references reviewed and updated.	02.13.18	05.18
2Q 2019 annual review: no significant changes; 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); references reviewed and updated.	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 of < 29 weeks.	12.12.19	
Seasonal coverage criteria are added to all indications; related AAP/CDC guidance is added to Appendix D.	05.01.20	08.20
2Q 2021 annual review: per prescribing information, added requirement for continued therapy that member will not reach 24 months of age at the start of RSV season; references reviewed and updated.	02.17.21	05.21
Per the CDC, added clarification that requests outside of the typical regional RSV season may be considered due to elevated interseasonal activity and inability to anticipate the likely spread, peak, or duration of activity with any certainty.	07.06.21	

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

be bound by the foregoing terms and conditions, in addition to the Site Use Agreement for Health Plans associated with Envolve Pharmacy Solutions.