Clinical Policy: Palivizumab (Synagis)

Reference Number: IN.CP.PHAR.16
Effective Date: 01.01.2022
Last Review Date: 12.21
Line of Business: 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 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.

RSV Season is defined as November 1st through March 31st. The season may be extended at the discretion of the Indiana Medicaid Office of Medicaid Policy and Planning (OMPP) based upon statewide virology data.

I. Initial Approval Criteria

A. Infants less than 12 months of age must meet one of the following:

1. Infants born preterm before 32 weeks gestation
2. Infants born with chronic lung disease (CLD) or bronchopulmonary dysplasia (BPD) (defined as: a oxygen requirement for at least 28 days after birth or those that developed an oxygen requirement)
3. Infants requiring medical therapy for hemodynamically significant heart disease or cardiomyopathies
4. Infants with neuromuscular disease or congenital abnormalities of the airways

Approval duration: up to 5 doses per RSV season

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B. Infants and Children less than 24 months of age must meeting one of the following:

1. Infants and children that required at least 28 days of supplemental oxygen after birth and who continue to require medical intervention (supplemental oxygen, chronic corticosteroid use or diuretic therapy)
2. Infants and children who will be profoundly immunocompromised during the RSV season (solid organ or hematopoietic stem cell transplant, chemotherapy, or other condition that leaves the infant profoundly immunocompromised, including those awaiting heart transplant)
3. Infants and children with evidence of hemodynamically significant coronary heart disease, cardiomyopathies, or pulmonary hypertension

Approval duration: up to 5 doses per RSV season

C. 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.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Member must meet all criteria for the age range on the date of this review.
2. Request is for RSV prophylaxis;
3. Member will not reach 24 months of age at the start of RSV season;

Approval duration: 1 dose for 30 days.

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BPD: bronchopulmonary dysplasia CLD: chronic lung disease of prematurity FDA: Food and Drug Administration

HHS: Health and Human Services
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.
- Traditionally, the RSV season was defined by consecutive weeks when RSV antigen-based tests exceeded 10% positivity; however, since 2008, laboratories have shifted away from antigen-based RSV testing, and since 2014 the majority of tests and RSV detections among consistently reporting laboratories are determined by polymerase chain reaction (PCR). The method that consistently captured the highest percentage of PCR detections for retrospectively characterizing RSV seasons was determined to be the retrospective slope 10 (RS10) method. This method uses a centered 5-week moving average of RSV detections normalized to a season peak of 1,000 detections. The season onset was defined as the second of 2 consecutive weeks when the slope, or normalized 5-week moving average of RSV detections between subsequent weeks, exceeded 10. The season offset was the last week when the standardized (normalized) detections exceeded the standardized detections at onset. The peak was the week with the most standardized detections. The season duration was the inclusive weeks between onset and offset. The RS10 method captures a high proportion of RSV PCR detections for retrospectively determining RSV seasonality, but cannot be used to determine seasonal onset and offset

in real time, and can only be employed after the season ends. Alternative statistical methods, including the tenfold baseline or 3% threshold methods might be used to determine seasonality in real time or near real time.

Appendix E: Dose Rounding Guidelines

IV. 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

V. Product Availability

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

VI. 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.

4. 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.
5. 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.
6. Rose EB, Wheatley A, Langley G, et al. Respiratory Syncytial Virus Seasonality — United States, 2014–2017. Morbidity and Mortality Weekly Report (MMWR). January 19, 2018. 67(2): 71-76. Available at: https://www.cdc.gov/mmwr/volumes/67/wr/mm6702a4.htm.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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; added that each dose of the Synagis prescription is written for RSV prophylaxis during current RSV season only; references reviewed and updated.	03.05.20	05.20
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; revised reference to HIM off-label use policy from HIM.PHAR.21 to HIM.PA.154; 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	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
For CLD requests, clarified chronic corticosteroid does not need to be systemic.	10.20.21	
Updated to meet IN Medicaid Moratorium requirement	12.2021	01/2022