Clinical Policy: Palivizumab (Synagis)

Reference Number: CP.PHAR.16
Effective Date: 08.01.09
Last Review Date: 05.24
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

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

Description

Palivizumab (Synagis®) is a recombinant humanized monoclonal antibody with anti-respiratory syncytial virus (RSV) activity.

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) and 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. Request is for RSV prophylaxis;
4. Member must use Beyfortus®, if available*, unless contraindicated or clinically significant adverse effects are experienced;
   ** For the 2023-2024 RSV season, supply issues are anticipated. Confirm supply constraints prior to bypassing this requirement (see Appendix D).*
5. Medical justification supports requests for RSV prophylaxis outside the identified season* duration for the specific region (*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 (e.g., September through May) by*

region may be considered. Traditionally RSV season onset was defined by consecutive weeks when RSV antigen-based tests exceeded 10% positivity. Due to the increased use of PCR testing, alternative statistical methods are used to determine seasonality in real time. Local and State health departments should be consulted to determine the real-time RSV season. Additional information on RSV trends by state can be found by visiting: https://www.cdc.gov/surveillance/nrevss/rsv/state.html.

6. Member has not been hospitalized with RSV disease during the current RSV season;
7. For the current RSV season, member has not previously received Beyfortus or other RSV monoclonal antibody or any RSV vaccine, including maternal RSV vaccination;
8. 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*

** Overlap of two seasons due to elevated interseasonal RSV activity does not preclude a member from receiving more than 5 consecutive doses, so long as doses are limited to 5 per season*

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

1. Diagnosis of chronic lung disease (CLD) of prematurity (i.e., BPD) defined as both of the following (a and b):
   a. Gestational age < 32 weeks;
   b. 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 corticosteroid therapy, bronchodilator therapy, or diuretic therapy within 6 months of the start of the RSV season;
3. Request is for RSV prophylaxis;
4. Member must use Beyfortus, if available*, unless contraindicated or clinically significant adverse effects are experienced;
   ** For the 2023-2024 RSV season, supply issues are anticipated. Confirm supply constraints prior to bypassing this requirement (see Appendix D).*
5. Medical justification supports requests for RSV prophylaxis outside the identified season* duration for the specific region (*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 (e.g., September through May) by region may be considered. Traditionally RSV season onset was defined by consecutive weeks when RSV antigen-based tests exceeded 10% positivity. Due to the increased use of PCR testing, alternative statistical methods are used to determine seasonality in real time. Local and State health departments should be consulted to determine the real-time RSV season. Additional information on RSV trends by state can be found by visiting:* https://www.cdc.gov/surveillance/nrevss/rsv/state.html.
6. Member has not been hospitalized with RSV disease during the current RSV season;
7. For the current RSV season, member has not previously received Beyfortus or other RSV monoclonal antibody or any RSV vaccine, including maternal RSV vaccination;
8. 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*

** Overlap of two seasons due to elevated interseasonal RSV activity does not preclude a member from receiving more than 5 consecutive doses, so long as doses are limited to 5 per 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. Request is for RSV prophylaxis;
3. Member must use Beyfortus, if available*, unless contraindicated or clinically significant adverse effects are experienced;
   ** For the 2023-2024 RSV season, supply issues are anticipated. Confirm supply constraints prior to bypassing this requirement (see Appendix D).*
4. Medical justification supports requests for RSV prophylaxis outside the identified season* duration for the specific region (*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 (e.g., September through May) by region may be considered. Traditionally RSV season onset was defined by consecutive weeks when RSV antigen-based tests exceeded 10% positivity. Due to the increased use of PCR testing, alternative statistical methods are used to determine seasonality in real time. Local and State health departments should be consulted to determine the real-time RSV season. Additional information on RSV trends by state can be found by visiting: https://www.cdc.gov/surveillance/nrevss/rsv/state.html.*
5. Member has not been hospitalized with RSV disease during the current RSV season;
6. For the current RSV season, member has not previously received Beyfortus or other RSV monoclonal antibody or any RSV vaccine, including maternal RSV vaccination;
7. 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)**

** Overlap of two seasons due to elevated interseasonal RSV activity does not preclude a member from receiving more than 5 consecutive doses, so long as doses are limited to 5 per season*

D. Anatomic Pulmonary Abnormalities, Neuromuscular Disorders, 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. Member must use Beyfortus, if available*, unless contraindicated or clinically significant adverse effects are experienced;
   ** For the 2023-2024 RSV season, supply issues are anticipated. Confirm supply constraints prior to bypassing this requirement (see Appendix D).*
4. Medical justification supports requests for RSV prophylaxis outside the identified season* duration for the specific region (*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 (e.g., September through May) by region may be considered. Traditionally RSV season onset was defined by consecutive weeks when RSV antigen-based tests exceeded 10% positivity. Due to the increased use of PCR testing, alternative statistical methods are used to determine seasonality in real time. Local and State health departments should be consulted to determine the real-time RSV season. Additional information on RSV trends by state can be found by visiting: https://www.cdc.gov/surveillance/nrevss/rsv/state.html.*
5. Member has not been hospitalized with RSV disease during the current RSV season;
6. For the current RSV season, member has not previously received Beyfortus or other RSV monoclonal antibody or any RSV vaccine, including maternal RSV vaccination;
7. 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*
** Overlap of two seasons due to elevated interseasonal RSV activity does not preclude a member from receiving more than 5 consecutive doses, so long as doses are limited to 5 per 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 both of the following (i and ii):
      i. Gestational age < 32 weeks
      ii. 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. Member must use Beyfortus, if available*, unless contraindicated or clinically significant adverse effects are experienced;
   ** For the 2023-2024 RSV season, supply issues are anticipated. Confirm supply constraints prior to bypassing this requirement (see Appendix D).*
5. Medical justification supports requests for RSV prophylaxis outside the identified season* duration for the specific region (*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 (e.g., September through May) by region may be considered. Traditionally RSV season onset was defined by consecutive weeks when RSV antigen-based tests exceeded 10% positivity. Due to the increased use of PCR testing, alternative statistical methods are used to determine seasonality in real time. Local and State health departments*

should be consulted to determine the real-time RSV season. Additional information on RSV trends by state can be found by visiting: https://www.cdc.gov/surveillance/nrevss/rsv/state.html.

6. Member has not been hospitalized with RSV disease during the current RSV season;
7. For the current RSV season, member has not previously received Beyfortus or other RSV monoclonal antibody or any RSV vaccine, including maternal RSV vaccination;
8. 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*

** Overlap of two seasons due to elevated interseasonal RSV activity does not preclude a member from receiving more than 5 consecutive doses, so long as doses are limited to 5 per 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. Member must use Beyfortus, if available*, unless contraindicated or clinically significant adverse effects are experienced;
   ** For the 2023-2024 RSV season, supply issues are anticipated. Confirm supply constraints prior to bypassing this requirement (see Appendix D).*
6. Medical justification supports requests for RSV prophylaxis outside the identified season* duration for the specific region (*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 (e.g., September through May) by region may be considered. Traditionally RSV season onset was defined by consecutive weeks when RSV antigen-based tests exceeded 10% positivity. Due to the increased use of PCR testing, alternative statistical methods are used to determine seasonality in real time. Local and State health departments should be consulted to determine the real-time RSV season. Additional information on RSV trends by state can be found by visiting: https://www.cdc.gov/surveillance/nrevss/rsv/state.html.*
7. Member has not been hospitalized with RSV disease during the current RSV season;
8. For the current RSV season, member has not previously received Beyfortus or other RSV monoclonal antibody or any RSV vaccine, including maternal RSV vaccination;
9. 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*

** Overlap of two seasons due to elevated interseasonal RSV activity does not preclude a member from receiving more than 5 consecutive doses, so long as doses are limited to 5 per season*

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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 meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Request is for RSV prophylaxis;
3. Member must use Beyfortus, if available*, unless contraindicated or clinically significant adverse effects are experienced;
   ** For the 2023-2024 RSV season, supply issues are anticipated. Confirm supply constraints prior to bypassing this requirement (see Appendix D).*
4. Member will not reach 24 months of age at the start of RSV season;
5. Medical justification supports requests for RSV prophylaxis outside the identified season* duration for the specific region (*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 (e.g., September through May) by region may be considered. Traditionally RSV season onset was defined by consecutive weeks when RSV antigen-based tests exceeded 10% positivity. Due to the increased use of PCR testing, alternative statistical methods are used to determine seasonality in real time. Local and State health departments should be consulted to determine the real-time RSV season. Additional information on RSV trends by state can be found by visiting: https://www.cdc.gov/surveillance/nrevss/rsv/state.html.*
6. Member has not yet received 5 Synagis doses in the current RSV season *(6 doses if cardio-pulmonary bypass);*
7. Member has not been hospitalized with RSV disease during the current RSV season;
8. For the current RSV season, member has not previously received Beyfortus or other RSV monoclonal antibody or any RSV vaccine, including maternal RSV vaccination;

9. 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)**

** Overlap of two seasons due to elevated interseasonal RSV activity does not preclude a member from receiving more than 5 consecutive doses, so long as doses are limited to 5 per season*

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 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.PA.154 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
HHS: Health and Human Services
RSV: respiratory syncytial virus

Appendix B: Therapeutic Alternatives

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Beyfortus® (nirsevimab)	**Prophylaxis - First RSV Season** Single IM injection of: • Weight < 5 kg: 50 mg • Weight ≥ 5 kg: 100 mg **Prophylaxis - Second RSV Season** Single 200 mg dose IM	First RSV Season: 1 dose Second RSV Season: 1 dose (2 doses per lifetime if member is at increased risk of severe disease)

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

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.

- The American Academy of Pediatrics (AAP) updated guidance for the 2021-2022 RSV season states the following:
  - For the current (2021-2022) fall and winter season, the AAP recommends beginning administration of palivizumab prophylaxis in all regions of the country at the usual time, regardless of whether an area experienced unusual interseasonal RSV activity. Initiating palivizumab prophylaxis to eligible infants similar to a typical winter season is consistent with AAP policy. The 2021-22 winter RSV season is considered a new season, rather than a continuation of the interseason spread in the spring and summer of 2021.
  - These considerations could reasonably lead to providing more than five consecutive doses of palivizumab to eligible children in some regions and less than five doses in other areas in the current fall and winter season. Although there is a paucity of data on the provision of more than 5 consecutive doses, there is no evidence of increased frequency or severity of adverse events with later doses in a 5-dose series nor with doses beyond 5 doses in the few published data. Given this information, together with the known efficacy and recent unpredictable epidemiology, the AAP recommends programmatic consideration of providing more than five consecutive doses from the atypical interseason period through the 2021-2022 winter season.
- The updated guidance provided by the AAP for the 2022-2023 RSV seasons states because of the continued variability in RSV circulation, the AAP continues to support the use of palivizumab in eligible patients in any region experiencing rates of RSV activity at any time in 2022 similar to a typical fall-winter season. The AAP continues to recommend programmatic consideration of providing more than 5 consecutive doses of palivizumab depending on the duration of the current RSV surge in a given region of the country.
- ACIP and AAP 2023 recommendations for the use of nirsevimab state the following regarding palivizumab:
  - If palivizumab was administered initially for the season and < 5 doses were administered, the infant should receive 1 dose of nirsevimab. No further palivizumab should be administered.
  - If palivizumab was administered in season 1 and the child is eligible for RSV prophylaxis in season 2, the child should receive nirsevimab in season 2, if available. If nirsevimab is not available, palivizumab should be administered as previously recommended.

- AAP frequently asked questions regarding nirsevimab state in the context of a limited supply of nirsevimab, CDC recommends providers suspend using nirsevimab in palivizumab-eligible children. If nirsevimab supply is inadequate, CDC recommends that providers suspend using nirsevimab in palivizumab-eligible children aged 8–19 months for the 2023–2024 RSV season. These children should receive palivizumab per American Academy of Pediatrics (AAP) recommendations. Nirsevimab should continue to be offered to American Indian and Alaska Native children aged 8–19 months who are not palivizumab-eligible and who live in remote regions, where transporting children with severe RSV for escalation of medical care is more challenging or in communities with known high rates of RSV among older infants and toddlers.

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

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 vials: 50 mg/0.5 mL, 100 mg/1 mL

VII. References

1. Synagis Prescribing Information. Gaithersburg, MD: MedImmune, LLC; November 2021. Available at https://www.synagis.com/synagis.pdf. Accessed January 9, 2024.
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: October 28, 2022. Accessed January 25, 2023.
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 January 25, 2023.

5. Kimberlin DW, Barnett ED, Lynfield R, et al. Red Book: 2021-2024 Report of the Committee on Infectious Diseases (32nd Edition). American Academy of Pediatrics; Section 3: Respiratory Syncytial Virus. Available at: https://publications.aap.org/redbook/book/347/Red-Book-2021-2024-Report-of-the-Committee-on. Accessed January 25, 2023.
6. 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.
7. 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.
8. 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.
9. Caserta MT, O'Leary ST, Munoz FM, et al. Palivizumab Prophylaxis in Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection. American Academy of Pediatrics: Technical Report. Pediatrics. July 2023; 152 (1): e2023061803.
10. 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.
11. 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.
12. 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.
13. Updated guidance: Use of Palivizumab Prophylaxis to Prevent Hospitalization From Severe Respiratory Syncytial Virus Infection During the 2022-2023 RSV Season. American Academy of Pediatrics. Pediatrics. November 17, 2022. Available at: https://www.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/interim-guidance-for-use-of-palivizumab-prophylaxis-to-prevent-hospitalization/. Accessed January 31, 2024.
14. ACIP and AAP Recommendations for Nirsevimab. Red Book Online. August 15, 2023. Available at: https://publications.aap.org/redbook/resources/25379/ACIP-and-AAP-Recommendations-for-Nirsevimab?searchresult=1?autologincheck=redirected. Accessed January 31, 2024.
15. AAP: Nirsevimab Frequently Asked Questions. Last updated January 12, 2024. Available at: https://www.aap.org/en/patient-care/respiratory-syncytial-virus-rsv-prevention/nirsevimab-frequently-asked-questions. Accessed January 31, 2024.

16. Health Alert Network CDCHAN-00499: Limited Availability of Nirsevimab in the United States—Interim CDC Recommendations to Protect Infants from Respiratory Syncytial Virus (RSV) during the 2023–2024 Respiratory Virus Season. October 23, 2023. Available at: https://emergency.cdc.gov/han/2023/han00499.asp. Accessed January 31, 2024.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
90378	Respiratory syncytial virus, monoclonal antibody, recombinant, for intramuscular use, 50 mg, each
S9562	Home injectable therapy, palivizumab or other monoclonal antibody for rsv, including administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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	
For CLD requests, clarified chronic corticosteroid does not need to be systemic.	10.20.21	
2Q 2022 annual review: no significant changes; Appendix D updated to include American Academy of Pediatrics (AAP) updated guidance for the 2021-2022 RSV season; references reviewed and updated.	02.21.22	05.22
Added clarification for approval duration with the following notation: "Overlap of two seasons due to elevated interseasonal RSV activity	05.31.22	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
does not preclude a member from receiving more than 5 consecutive doses, so long as doses are limited to 5 per season."		
Appendix D updated to include AAP updated guidance for the 2022-2023 RSV seasons; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	09.07.22	
2Q 2023 annual review: for CLD added bronchodilator therapy as an additional option to confirm appropriateness of therapy in the second year of life per AAP guidance; references reviewed and updated.	01.04.23	05.23
Added redirection to Beyfortus per ACIP and AAP recommendations; clarified requirement for medical justification for use "outside" the typical RSV season by allowing region-by-region identified RSV season; added the following requirement: "for the current RSV season, member has not previously received Beyfortus or other RSV monoclonal antibody or any RSV vaccine, including maternal RSV vaccination."	10.26.23	11.23
2Q 2024 annual review: no significant changes; updated Appendix D with AAP recommendations in the context of a limited supply of nirsevimab; added the following notation to clarify Beyfortus redirection if available: "For the 2023-2024 RSV season, supply issues are anticipated. Confirm supply constraints prior to bypassing this requirement (see Appendix D)."; references reviewed and updated.	01.09.24	05.24

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.