Drug and Biologic Coverage Policy

Effective Date.....**12/15/2024**
Coverage Policy Number.....**IP0321**

Palivizumab

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for **Synagis®** (palivizumab) intramuscular injection.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Palivizumab (Synagis) is considered medically necessary when ONE of the following is met:

1. **Respiratory Syncytial Virus (RSV), Prevention in an Individual with Chronic Lung Disease.** Individual meets **ONE** of the following criteria:
    A. Individual is less than 12 months of age at the start of the RSV season and meets **BOTH** of the following criteria:
        i. Individual was born before 32 weeks, 0 days gestation
        ii. Individual required supplemental oxygen for at least the first 28 days after birth
    B. Individual is 12-24 months of age at the start of RSV season and **ALL** of the following criteria:
        i. Individual was born before 32 weeks, 0 days gestation
        ii. Individual required supplemental oxygen for at least the first 28 days after birth

iii. Individual required medical support (chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) during the 6 month period prior to the start of the RSV season

2. **Respiratory Syncytial Virus (RSV), Prevention in an Individual with Congenital Heart Disease.** Individual meets **ALL** of the following criteria:
    A. Individual is less than 12 months of age at the start of the RSV season
    B. Individual meets **ONE** of the following criteria:
        i. Individual has hemodynamically significant cyanotic congenital heart disease
        ii. Individual meets **ALL** of the following:
            a. Individual has acyanotic heart disease
            b. Individual is receiving medication to control heart failure
            c. Individual will require cardiac surgical procedures
        iii. Individual has moderate to severe pulmonary hypertension
        iv. Individual meets **BOTH** of the following:
            a. Individual has hemodynamically significant congenital heart defects that have been adequately corrected by surgery
            b. Individual continues to require medication for congestive heart failure
    C. Medication is being prescribed by, or in consultation with, a pediatric cardiologist, neonatologist, or pulmonologist

3. **Respiratory Syncytial Virus (RSV), Prevention in an Individual Born Prematurely.** Individual meets **BOTH** of the following criteria:
    A. Individual is less than 12 months of age at the start of RSV season
    B. Individual was born before 29 weeks, 0 days gestation

4. **Respiratory Syncytial Virus (RSV), Prevention in an Individual with Anatomic Pulmonary Abnormalities or a Neuromuscular Disorder.** Individual meets **BOTH** of the following criteria:
    A. Individual is less than 12 months of age at the start of RSV season
    B. Individual has a congenital abnormality of the airway or a neuromuscular disease (for example, cerebral palsy, muscular dystrophy, neurological diseases of the brain and spinal cord [Tay Sachs, spinal muscular dystrophy]) that compromises the handling of respiratory secretions

5. **Respiratory Syncytial Virus (RSV), Prevention in an Immunocompromised Individual.** Individual meets **ALL** of the following criteria:
    A. Individual is less than 24 months of age at the start of RSV season
    B. Individual is/will be profoundly immunocompromised (for example, severe combined immunodeficiency or severe acquired immunodeficiency syndrome) during the RSV season
    C. Medication is being prescribed by, or in consultation with, an immunologist or an infectious diseases specialist

6. **Respiratory Syncytial Virus (RSV), Prevention in an Individual with Cardiac Transplant.** Individual meets **ALL** of the following criteria:
    A. Individual is less than 24 months of age at the start of the RSV season
    B. Individual has undergone or will undergo cardiac transplantation during the current RSV season
    C. Medication is being prescribed by, or in consultation with, a cardiologist, neonatologist, pulmonologist, or transplant physician

7. **Respiratory Syncytial Virus (RSV), Prevention in an Individual with Cystic Fibrosis.** Individual meets **BOTH** of the following criteria:
    A. **ONE** of the following:
        i. Individual is less than 12 months of age at the start of RSV season and **ONE** of the following criteria:
            a. Individual was born before 32 weeks, 0 days gestation and supplemental oxygen for at least the first 28 days after birth
            b. Nutritional compromise as evidenced by weight for length less than the 10th percentile on a pediatric growth chart
        ii. Individual is 12-24 months of age at the start of RSV season and **ONE** of the following criteria:
            a. Manifestations of severe lung disease (history of hospitalization for pulmonary exacerbation, abnormal chest x-ray or chest computed tomography [CT] SCAN)
            b. Nutritional compromise as evidenced by weight for length less than the 10th percentile on a pediatric growth chart
    B. Medication is being prescribed by, or in consultation with pulmonologist

8. **Respiratory Syncytial Virus (RSV), Prevention in an Alaska Native or American Indian (Navajo, White Mountain Apache).** Individual meets the following criteria:
    A. Individual is less than 12 months of age at the start of RSV season

    Dosing. Dose of 15 mg/kg given intramuscularly once monthly during the RSV season.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

An additional dose of palivizumab following cardiac bypass or extra-corporeal membrane oxygenation for infants and children less than 24 months of age who are receiving RSV prophylaxis and will continue to require prophylaxis following surgery is covered.

Authorization Duration

Initial approval duration is up to 5 months.

Reauthorization approval duration: An additional dose of palivizumab following cardiac bypass or extra-corporeal membrane oxygenation for infants and children less than 24 months of age who are receiving RSV prophylaxis and will continue to require prophylaxis following surgery is covered.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

1. **Respiratory Syncytial Virus (RSV), Prevention in an Individual with Cystic Fibrosis <u>Who Does Not Meet Any of the policy statements listed above</u>.** The AAP guidelines for RSV note that routine use of Synagis prophylaxis in patients with cystic fibrosis, including neonates diagnosed with cystic fibrosis by newborn screening, is not recommended unless

other indications are present.[4] Available studies indicate the incidence of RSV hospitalization in children with cystic fibrosis is uncommon and unlikely to be different from children without cystic fibrosis.[3] A Cochrane Review identified one trial (presented in poster/abstract form) eligible for their review of Synagis prophylaxis in children with cystic fibrosis.[5] In this prospective, double-blind, placebo-controlled, multi-center study, 14.1% vs. 14.9% of Synagis and placebo-treated patients, respectively were hospitalized within the first 6 months, and only one patient in each group was identified with RSV infection. There were no deaths in either group of patients during the first 6 months follow-up; this outcome was not reported at 12 months follow-up.

2. **Respiratory Syncytial Virus (RSV), Prevention in an Individual with Down Syndrome <u>Who Does Not Meet Any of the policy statements listed above.</u>** Data suggest that children with Down syndrome have a slightly higher hospitalization rate for RSV, but the absolute number of hospitalizations is small, and a number of children with Down syndrome are at increased risk because of other qualifying risk factors (for example, congenital heart disease, abnormalities of the respiratory tract, muscle dystonia).[3]

3. **Respiratory Syncytial Virus (RSV), Treatment of Disease.** There are limited data investigating Synagis for the treatment of established RSV infections. Passive antibody administration is not effective in treatment of RSV disease and is not approved or recommended for this indication.[3,4] If any infant or young child receiving monthly Synagis prophylaxis experiences a breakthrough RSV hospitalization, monthly prophylaxis should be discontinued because of the extremely low likelihood of a second RSV hospitalization (< 0.5%).[4]

4. **Use in an individual who has Received Beyfortus (nirsevimab-alip intramuscular injection) in the Same RSV Season.** Synagis should not be administered to infants who have already received Beyfortus for the same RSV season.[10,11,12] However, if Synagis was initially administered for the season, and < 5 doses were administered, the infant should receive one dose of Beyfortus.[12] No further Synagis should be administered. If Synagis was administered in the first RSV season, and the child is eligible for RSV prophylaxis in the second RSV season, the child should receive Beyfortus in the second RSV season, if available. <u>Note</u>: The RSV season is generally 6 months in duration.

Background

OVERVIEW

Synagis, a respiratory syncytial virus (RSV) F protein inhibitor monoclonal antibody, is indicated for the **prevention of serious lower respiratory tract disease caused by RSV in children at high risk of RSV disease**.[1] Safety and efficacy were established in children with bronchopulmonary dysplasia, infants with a history of premature birth, and children with hemodynamically significant congenital heart disease.

The safety and efficacy of Synagis for the treatment of RSV have not been established.[1] The recommended dose is 15 mg/kg intramuscularly once monthly (every 30 days). The first dose of Synagis should be administered prior to commencement of the RSV season and the remaining doses should be administered monthly throughout the RSV season.

RSV Seasonality

The Centers for Disease Control and Prevention National Respiratory and Enteric Virus Surveillance System provides reports determining RSV seasonality, nationally and by region. The COVID-19 pandemic disrupted RSV seasonality from 2020 to 2022.[2] To describe US RSV seasonality during pre-pandemic and pandemic periods, polymerase chain reaction (PCR) test results reported to the

National Respiratory and Enteric Virus Surveillance System during July 2017 through February 2023 were analyzed. Seasonal RSV epidemics were defined as the weeks during which ≥ 3% of PCR test results were positive for RSV. Nationally, pre-pandemic seasons (2017 to 2020) began in October, peaked in December, and ended in April. During 2020/2021, the typical winter RSV epidemic did not occur. The 2021/2022 season began in May, peaked in July, and ended in January. The 2022/2023 season started (June) and peaked (November) later than the 2021/2022 season, but earlier than pre-pandemic seasons. In both pre-pandemic and pandemic periods, epidemics began earlier in Florida and the southeast and later in regions further north and west. Although the timing of the 2022/2023 season suggests that seasonal patterns are returning toward those observed in pre-pandemic years, off-season RSV circulation may continue.

Guidelines

The American Academy of Pediatrics (AAP) Policy Statement on the Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for RSV Infection was updated in July 2023.[3] Additionally, the AAP Red Book was updated in 2024.[4] The AAP Red Book states that Synagis may be administered if Beyfortus (nirsevimab-alip intramuscular injection) is not available. If Beyfortus becomes available during the RSV season and before the 5th dose of Synagis, a single Beyfortus dose should be given and no additional Synagis doses should be administered. Data are insufficient to justify a recommendation for routine use of prophylaxis in patients with Down syndrome or among those with cystic fibrosis unless other indications are present. National Perinatal Association 2024 RSV prevention clinical practice guidelines reaffirm the AAP policy statement recommendations.

The Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP) [August 25, 2023] recommend one dose of Beyfortus for all infants < 8 months of age born during or entering their first RSV season (50 mg for infants < 5 kg and 100 mg for infants ≥ 5 kg).[11] ACIP recommends one dose of Beyfortus (200 mg, administered as two 100-mg injections given at the same time at different injection sites) for infants and children 8 to 19 months of age who are at increased risk for severe RSV disease and entering their second RSV season.

The ACIP and AAP have published considerations for the 2023/2024 RSV season with regard to Synagis vs. Beyfortus in high-risk infants (August 15, 2023).[12] In general, the joint recommendations mirror the ACIP recommendations above. In addition, if Beyfortus is administered, Synagis should not be administered later that season. If Synagis was initially administered for the season and < 5 doses were administered, the infant should receive one dose of Beyfortus. No further Synagis should be administered. If Synagis was administered in the first RSV season, and the child is eligible for RSV prophylaxis in the second RSV season, the child should receive Beyfortus in the second RSV season, if available. An additional recommendation regarding Beyfortus is that in healthy infants born at the end of their first RSV season, who did not receive Beyfortus and are < 8 months of age entering their second RSV season, a single dose of Beyfortus may be given.

On October 23, 2023, the CDC issued a Health Alert Network Health Advisory to provide options for clinicians to protect infants from RSV in the context of a limited supply of Beyfortus.[14] In the context of limited supply during the 2023/2024 RSV season, CDC recommends prioritizing available Beyfortus 100 mg doses for infants at the highest risk for severe RSV disease: young infants (< 6 months of age) and infants with underlying conditions that place them at highest risk for severe RSV disease. Recommendations for using 50 mg doses remain unchanged at this time. The CDC further recommends that providers suspend using Beyfortus in Synagis-eligible children who are 8 to 19 months of age for the 2023/2024 RSV season. These children should receive Synagis according to the AAP recommendations. Beyfortus should continue to be offered to American Indian and Alaska Native children aged 8 to 19 months who are not Synagis-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.

RSV Seasonality and Recommendations
Although typical RSV seasonality in the US occurs primarily in the fall and winter months, there was a rapid decrease in RSV infections in the US beginning in March 2020 following non-pharmacologic interventions to prevent COVID-19.[6] RSV activity remained very low through the traditional 2020-2021 fall-winter season but began to increase in spring 2021 and cases rose to a level similar to a fall-winter season throughout the US over the summer and fall of 2021.[7] This was a deviation from usual RSV epidemiology.[6,7] Because of the change in RSV circulation, AAP strongly supported consideration for use of Synagis in eligible patients during the interseasonal spread of RSV.[6] According to a statement released by AAP on December 17, 2021, the 2021-2022 winter RSV season is considered a new season, rather than a continuation of the interseason spread in the spring and summer of 2021.

As of July 2022, RSV activity in the US remains variable by region but is increasing in some parts of the country.[7] Due to the shift in RSV seasonality noted in 2021 and the current regional rise in interseason RSV cases, the AAP continues to support the use of Synagis in eligible infants in any region experiencing rates of RSV activity at any time in 2022 similar to a typical fall-winter season. The standard administration of Synagis, 5 consecutive monthly doses, is recommended by the AAP to provide serum levels associated with protection for 6 months, the length of a typical RSV season. The AAP will continue to monitor the interseasonal trends and update this guidance as needed if the RSV season extends longer than 6 months.

The start of the RSV season has historically been defined as case positivity rate of 10% by antigen or PCR testing.[8] However, a 10% threshold for PCR tests has been found to be imprecise for characterizing the RSV season. Therefore, other thresholds have been used for PCR tests. A 3% threshold has been found to be a simple method to assess the onset and offset of the RSV season (defining the RSV season onset as the first of 2 consecutive weeks when the weekly percentage of positive tests for RSV is > 3% and season offset as the last week that the percentage of positive tests is >3%).[8,9] A 10% threshold appears reasonable for antigen testing.

Coding Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
90378	Respiratory syncytial virus, monoclonal antibody, recombinant, for intramuscular use, 50 mg, each

References

1. Synagis® [prescribing information]. Waltham, MA: Sobi.; November 2021.
2. Hamid S, Winn A, Parikh R et al. Seasonality of respiratory syncytial virus – United States, 2017-2023. *MMWR Morbid Mortal Wkly Rep.* 2023; 72:355-361.

3. Caserta MT, O'Leary ST, Munoz FM, Ralston SL, and the Committee on Infectious Diseases. Technical Report. Palivizumab prophylaxis in infants and young children at increased risk of hospitalization for respiratory syncytial virus infection. Pediatrics. 152;1: e2023061803.
4. Respiratory Syncytial Virus. In: Kimberlin DW, Banerjee R, Barnett ED, Lynfield R, Sawyer MH (Eds). Red Book: 2024-2027 Report of the Committee of Infectious Diseases. 33rd Edition, Itasca, IL: American Academy of Pediatrics; 2024.
5. Robinson KA, Odelola OA, Saldanha IJ. Palivizumab for prophylaxis against respiratory syncytial virus infection in children with cystic fibrosis. Cochrane Database Syst Rev. 2016;7:CD007743. doi: 10.1002/14651858.CD007743.pub6.
6. American Academy of Pediatrics. Updated guidance: Use of palivizumab prophylaxis to prevent hospitalization from severe respiratory syncytial virus infection during the 2021-2022 RSV season. Updated December 17, 2021. 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 on August 19, 2024.
7. American Academy of Pediatrics. Updated guidance: Use of palivizumab prophylaxis to prevent hospitalization from severe respiratory syncytial virus infection during the 2022-2023 RSV season. Updated 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 on August 11, 2023.
8. Midgley CM, Haynes AK, Baumgardner C, et al Determining the seasonality of respiratory syncytial virus in the United States: The impact of increased molecular testing. JID. 2017; 216:345-355.
9. Ambrose CS, Steed LL, Brandon M, et al. National and regional modeling of distinct RSV seasonality thresholds for antigen and PCR testing in the US. J Clin Virol. 2019; 120:68-77.
10. Beyfortus™ injection [prescribing information]. Swiftwater, PA: Sanofi-Pasteur; February 2024.
11. Jones JM, Duttra KEF, Prill MM, et al. Use of nirsevimab for the prevention of respiratory syncytial virus disease among infants and young children: recommendations of the Advisory Committee on Immunization Practices – United States, 2023. MMWR; 2023; 72:34:920-925. Available at: https://www.cdc.gov/mmwr/volumes/72/wr/pdfs/mm7234a4-H.pdf. Accessed on: September 5, 2023.
12. ACIP and AAP recommendations for Nirsevimab. August 15, 2023. Available at: https://publications.aap.org/redbook/resources/25379?autologincheck=redirected. Accessed on: August 19, 2024.
13. The Centers for Disease Control and Prevention. 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. Published October 23, 2023. Available at: https://emergency.cdc.gov/han/2023/han00499.asp. Accessed on: October 24, 2023.
14. Goldstein M, Hopkins B, Kadri M, et al. National Perinatal Association 2024 respiratory syncytial virus (RSV) prevention clinical practice guideline: clinical presentation, prevention strategies, and social impacts in children: an evidence-based interdisciplinary collaboration. Neonatology Today. 2024;19(1):9-38.

Revision Details

Type of Revision	Summary of Changes	Date
Selected Revision	**Updated** review date, disclaimer, refreshed background and references, addition of change history.	12/15/2024

The policy effective date is in force until updated or retired.