PRIOR AUTHORIZATION POLICY

POLICY: Synagis Prior Authorization Policy
- Synagis® (palivizumab intramuscular injection – Sobi)

REVIEW DATE: 08/21/2024; selected revision 10/02/2024

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 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]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Synagis. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

Because five monthly doses of Synagis at 15 mg/kg per dose will provide more than 6 months of serum Synagis concentrations for most infants, administration of more than five monthly doses is not recommended within the continental US. Children who qualify for five monthly doses of Synagis should receive the first dose at the time of onset of the RSV season. For qualifying infants born during the RSV season, fewer than five monthly doses will be needed to provide protection until the RSV season ends in their region (maximum of five monthly doses). For the purposes of this policy, RSV season onset is defined as the first 2 consecutive weeks when the percentage of positive tests for RSV is > 3% by PCR. RSV season offset is defined as the last week that the percentage of positive tests for RSV is > 3% by PCR.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Synagis is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Respiratory Syncytial Virus (RSV), Prevention in a Patient with Chronic Lung Disease**. Approve for a maximum of 5 months during the RSV season if the patient meets ONE of the following (A or B):
   - **A)** Patient is < 12 months of age at the start of the RSV season and meets BOTH of the following (i and ii):
     - **i.** Patient was born at < 32 weeks, 0 days gestation; AND
     - **ii.** Patient required > 21% oxygen for at least 28 days after birth; OR
   - **B)** Patient is ≥ 12 months of age but < 24 months of age at the start of the RSV season and meets ALL of the following (i, ii, and iii):
     - **i.** Patient was born at < 32 weeks, 0 days gestation; AND
     - **ii.** Patient required > 21% oxygen for at least 28 days after birth; AND
     - **iii.** Patient has required medical therapy (i.e., supplemental oxygen, diuretic therapy, or chronic corticosteroid therapy) during the 6 months before the start of the second RSV season.

2. **Respiratory Syncytial Virus (RSV), Prevention in a Patient with Congenital Heart Disease.** Approve for a maximum of 5 months during the RSV season if the patient meets ALL of the following (A, B, and C):
   - **A)** Patient is < 12 months of age at the start of the RSV season; AND
   - **B)** According to the prescriber, patient meets ONE of the following (i, ii, iii, or iv):
     - **i.** Patient is considered to have hemodynamically significant cyanotic congenital heart disease; OR
     - **ii.** Patient meets ALL of the following (a, b, and c):
       - **a)** Patient has acyanotic heart disease; AND
       - **b)** Patient is receiving medication to control heart failure; AND

c) Patient will require cardiac surgical procedures; OR

iii. Patient has moderate to severe pulmonary hypertension; OR

iv. Patient meets BOTH of the following (a and b):

a) Patient has lesions that have been adequately corrected by surgery; AND

b) Patient continues to require medication for congestive heart failure; AND

C) Synagis is prescribed by or in consultation with a cardiologist or intensivist.

3. **Respiratory Syncytial Virus (RSV), Prevention in a Patient Born Prematurely.** Approve for a maximum of 5 months during the RSV season if the patient meets BOTH of the following (A and B):
   A) Patient is < 12 months of age at the start of the RSV season; AND
   B) Patient was born before 29 weeks, 0 days gestation (≤ 28 weeks, 6 days gestation).

Other Uses with Supportive Evidence

4. **Respiratory Syncytial Virus (RSV), Prevention in a Patient with Anatomic Pulmonary Abnormalities or a Neuromuscular Disorder.** Approve for a maximum of 5 months during the RSV season if the patient meets BOTH of the following (A and B):
   A) Patient is < 12 months of age at the start of the RSV season; AND
   B) According to the prescriber, the patient's condition compromises the handling of respiratory secretions.

5. **Respiratory Syncytial Virus (RSV), Prevention in an Immunocompromised Patient.** Approve for a maximum of 5 months during the RSV season if the patient meets ALL of the following (A, B, and C):
   Note: Examples of immunocompromised patients include those receiving chemotherapy and those with hematopoietic stem cell transplant or solid organ transplant.
   A) Patient is < 24 months of age at the start of the RSV season; AND
   B) According to the prescriber, the patient is/will be profoundly immunocompromised during the RSV season; AND
   C) Synagis is prescribed by or in consultation with an immunologist or an infectious diseases specialist.

6. **Respiratory Syncytial Virus (RSV), Prevention in a Patient with Cardiac Transplant.** Approve for a maximum of 5 months during the RSV season if the patient meets ALL of the following (A, B, and C):
   Note: A patient with cardiac transplant may also be immunocompromised. In a patient who does not meet criteria for cardiac transplant below, please see criterion 5 above (Respiratory Syncytial Virus [RSV], Prevention in an Immunocompromised Patient).
   A) Patient is < 24 months of age at the start of the RSV season; AND
   B) Patient has undergone or will undergo cardiac transplantation during the current RSV season; AND
   C) Synagis is prescribed by or in consultation with a cardiologist, intensivist, or transplant physician.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Synagis is not recommended in the following situations:

1. **Respiratory Syncytial Virus (RSV), Prevention in a Patient with Cystic Fibrosis Who Does Not Meet Any of the Approval Criteria.** 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 of follow-up; this outcome was not reported at 12 months of follow-up.

2. **Respiratory Syncytial Virus (RSV), Prevention in a Patient with Down Syndrome Who Does Not Meet Any of the Approval Criteria.** 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 (e.g., 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 a Patient 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.
   Note: The RSV season is generally 6 months in duration.

5. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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