Synagis® (palivizumab)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Synagis® (palivizumab) drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines and clinical studies. Synagis is a recombinant humanized monoclonal antibody which exhibits neutralizing and fusion-inhibitory activity against respiratory syncytial virus (RSV). Synagis is approved by the Food and Drug Administration (FDA) for the prevention of serious lower respiratory tract disease caused by RSV in pediatric patients considered to be high risk for developing complications from RSV disease. Safety and efficacy were established in infants with bronchopulmonary dysplasia ([BPD], now more commonly referred to as chronic lung disease of prematurity [CLD]), infants with a history of premature birth, and children with hemodynamically significant congenital heart disease (CHD). The primary benefit of immunoprophylaxis with Synagis is a reduction in RSV related hospitalizations; no prospective, randomized controlled trials have demonstrated a significant reduction in mortality or long-term respiratory outcomes. The safety and efficacy of Synagis have not been established for the treatment of RSV disease. Synagis is administered by intramuscular injection at a dose of 15 mg/kg once every 30 days during RSV season.

POLICY

Criteria for Initial Approval

I. Synagis® (palivizumab) may be considered **medically necessary** for use as immunoprophylaxis for RSV in infants who were born at less than 29 weeks' gestation (28 weeks, 6 days and earlier) **AND** who are younger than 12 months of age at the onset of RSV season

   Approval will be for a **maximum of 5 doses.**

II. Synagis® (palivizumab) may be considered **medically necessary** for use as immunoprophylaxis for RSV in preterm infants and children born before 32 weeks gestation (31 weeks, 6 days and earlier) with chronic lung disease of prematurity (CLD) defined as a greater than 21% oxygen requirement for at least 28 days after birth when the following criteria are met:

- The patient is younger than 12 months of age at the onset of RSV season
  OR
- The patient is younger than 24 months of age at the start of RSV season **AND** has continued to require medical therapy (i.e., supplemental oxygen, diuretic therapy, chronic corticosteroid therapy) during the 6-month period prior to the start of the RSV season

Approval will be for a **maximum of 5 doses.**

III. Synagis® (palivizumab) may be considered **medically necessary** for use as immunoprophylaxis for RSV in infants and children with congenital heart disease (CHD) who are less than 12 months of age at the onset of RSV season when the following criteria are met:
  - The patient has a diagnosis of hemodynamically significant congenital heart disease (CHD) including **ONE** of the following:
    - Acyanotic heart disease for which the patient is receiving medication to control congestive heart failure **AND** will require cardiac surgical procedures
    - Moderate to severe pulmonary hypertension
    - Cyanotic heart disease in consultation with a pediatric cardiologist

Approval will be for a **maximum of 5 doses.***

***For children with heart disease meeting the above criteria, an additional postoperative dose of palivizumab may be considered **medically necessary** following cardiopulmonary bypass or the conclusion of extracorporeal membrane oxygenation.

IV. Synagis® (palivizumab) may be considered **medically necessary** for use as immunoprophylaxis for RSV in infants and children younger than 24 months of age at the onset of RSV season that have undergone cardiac transplantation during RSV season.

Approval will be for a **maximum of 5 doses.**

V. Synagis® (palivizumab) may be considered **medically necessary** for use as immunoprophylaxis for RSV in infants with congenital abnormalities of the airways or neuromuscular condition that compromises the handling of secretions when the patient is younger than 12 months of age at the onset of RSV season.

Approval will be for a **maximum of 5 doses**

VI. Synagis® (palivizumab) may be considered **medically necessary** for use as immunoprophylaxis for RSV in infants and children younger than 24 months of age who are profoundly immunocompromised (e.g. including those who have undergone solid organ transplant, undergoing hematopoietic stem cell transplant, receiving chemotherapy) during the RSV season.

Approval will be for a **maximum of 5 doses.**

VII. Synagis® (palivizumab) may be considered **medically necessary** for use as immunoprophylaxis for RSV in infants and children with a diagnosis of cystic fibrosis and meet the following criteria:

- The patient is less than 12 months of age at the onset of RSV season and have **ONE** of the following:
  - Clinical evidence of CLD
  - Nutritional compromise

OR

- The patient is less than 24 months of age at the onset of RSV season and have **ONE** of the following:
  - Manifestations of severe lung disease defined as a previous hospitalization for pulmonary exacerbation in the first year of life or an abnormal chest radiography or chest computed tomography that persists when stable
  - Weight for length less than 10th percentile

Approval will be for a **maximum of 5 doses.**

VIII. Synagis is considered **not medically necessary** for patients who do not meet the criteria set forth above.

Other

For all off-season Synagis requests, authorization of 1 dose per request, up to a maximum of 5 doses per RSV season, may be granted if the RSV activity for the requested region is ≥ 3% (with real-time polymerase chain reaction (PCR) test) within 2 weeks of the intended dose according to the CDC National Respiratory and Enteric Virus Surveillance System (NREVSS). The local health department or the CDC NREVSS will be consulted to assess the RSV activity for that region (http://www.cdc.gov/surveillance/nrevss/rsv/index.html). Initial Criteria for Approval criteria and Quantity/Dosing limits will apply.

Wellmark Synagis Season for 2022-2023 will be November 1, 2022 to April 30, 2023. For the current 2022-2023 fall and winter season, the American Academy of Pediatrics (AAP) supports initiating the standard palivizumab regimen (five consecutive monthly doses) for eligible infants in regions of the United States with interseasonal rates of RSV activity similar to those in a typical fall-winter season. During the COVID-19 pandemic, RSV has not followed its typical seasonality of late fall through spring, leading the AAP to support use of the monoclonal antibody at other times of the year if activity is comparable to a regular season. Currently, virus activity varies by region. Please note, any doses received prior to November 1st will not count towards the 2022-2023 season's 5 dose total.

Dosage and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Synagis should be administered intramuscularly at a dose of 15 mg/kg once per month beginning prior to the onset of the RSV season, which typically occurs in November. Because 5 monthly doses of Synagis will provide more than 6 months of serum Synagis concentrations above the desired serum concentration for most infants, administration of more than 5 monthly doses is not recommended within the continental United States.

Quantity Limits Apply: 5 doses per RSV season

CLINICAL RATIONALE

Each year in the United States an estimated 75,000 to 125,000 infants and susceptible toddlers are hospitalized for RSV related illness and 200 to 400 deaths are attributed to RSV. Hospitalization rates are highest in the first year of life. In addition to hospitalizations, RSV illness results in a significant number of both emergency department and pediatric office visits.

While most children will have been exposed to RSV by the time they reach two years of age, the illness generally manifests as an upper respiratory infection and rarely poses significant harm. Children born premature and those with specific medical conditions have been identified as being most vulnerable to severe RSV infection, which can require hospitalization. Although severe disease occurs more frequently among high risk infants and toddlers, the majority of RSV-related hospitalizations and deaths occur in children without an underlying high-risk condition.

At this time, there is not a vaccine to prevent RSV and treatment primarily involves supportive measures. In the United States, Synagis® (palivizumab) is the only product available as immunoprophylaxis. In studies, palivizumab has been shown to reduce hospitalization rates in high-risk patient populations. According to the two large randomized controlled trials, for which palivizumab approval is based, palivizumab demonstrated a reduction in hospitalization rates by ~50 percent, which was associated with numbers needed to treat (NNT) of 16 (for those born premature), 20 (for those with chronic lung disease of prematurity or CLD), and 23 (for those with hemodynamically significant congenital heart disease or CHD). There is no evidence palivizumab affects mortality associated with RSV infection. Given the high cost of immunoprophylaxis with palivizumab, identifying those most likely to benefit and timing the administration to align with the RSV season is critical to ensure its most cost-effective use. The American Academy of Pediatrics (AAP) has established recommendations for palivizumab, defining those most likely to benefit based on the available evidence; their recommendations serve as the foundation for this drug policy. In July 2014 the AAP released updated guidance that was considerably more restrictive in nature. The Academy makes clear their recommendations were not based on cost, but instead "driven by the ***limited clinical benefit*** derived from palivizumab prophylaxis". In September 2017, the Committee on Infectious Diseases and the Subcommittee on Bronchiolitis reviewed new data and reaffirmed the 2014 AAP recommendations. The 2014 AAP recommendations were reaffirmed again in February 2019.

In most areas of the United States, the usual time for the beginning of the RSV outbreaks occurs in November/December, peaking in January/February, with outbreaks ending in March/April. RSV season may commence earlier or persist later in certain communities. Variations in the timing and intensity of RSV from season to season and among different communities may arise from several factors including weather conditions that affect virus virility, and population factors such as population density and immunity, which may affect the likelihood of transmission.

Regardless of the month when the first dose is administered, the AAP guidelines make clear the recommendation for a maximum of 5 doses for the entire RSV season. Results from clinical trials indicate that 5 monthly doses provide more than 6 months of protective serum antibody concentration, which provides adequate coverage for an RSV season. Specifically, the AAP states the following: "For qualifying infants who require 5 doses, a dose beginning in November and continuation for a total of 5 monthly doses will provide protection for most infants **through April** and is recommended for most areas of the United States." Administration of more than 5 monthly doses is **NOT** recommended within the continental United States.

Due to the small probability of a second RSV hospitalization occurring in the same season (<0.5%), immunoprophylaxis with Synagis should be discontinued in any infant or child who experiences a breakthrough RSV hospitalization.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

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

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POLICY HISTORY

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