Medical Drug Clinical Criteria

Subject:	Synagis (palivizumab)		
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Overview

This document addresses the use of Synagis (palivizumab), a monoclonal antibody approved by the Food and Drug Administration for prevention of serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) infection in select pediatric individuals.

Randomized placebo-controlled clinical trials have demonstrated the safety and efficacy of Synagis in reducing hospitalizations due to RSV infection and in reductions in other measures of RSV infection severity for a very specific group of infants and children. Epidemiologic data indicate that the risk of severe RSV infection most likely to require hospitalization is greater in the presence of risk factors.

In 2014, the American Academy of Pediatrics (AAP) issued updated guidelines regarding the use of immune prophylaxis for RSV. AAP reaffirmed this guidance in 2019. A summary of the AAP RSV guidance is as follows:

Preterm Infants without Chronic Lung Disease (CLD) of Prematurity or Congenital Heart Disease (CHD)
• Infants born before 29 weeks, 0 days gestation in the first year of life
Preterm Infants with CLD
• Infants born before 32 weeks, 0 days gestation and a requirement for >21% oxygen for at least 28 days after birth in the first year of life
Infants with CHD
• Prophylaxis may be administered in first year of life to certain infants with hemodynamically significant heart disease • Consultation with a cardiologist if recommended for patients with cyanotic heart disease for prophylaxis decisions
Children with Anatomic Pulmonary Abnormalities or Neuromuscular Disorder
• Prophylaxis may be considered in first year of life to children with pulmonary abnormality or neuromuscular disease that impairs the ability to clear secretions from the upper airways
Immunocompromised Children
• Prophylaxis may be considered in children under 24 months who will be profoundly immunocompromised during the RSV season
Children with Down Syndrome
• Insufficient data available to routinely recommend prophylaxis
Children with Cystic Fibrosis
• Insufficient data available to routinely recommend prophylaxis
Timing of Prophylaxis for Alaska Native and American Indian Infants
• Greater flexibility in use of prophylaxis as a result of potentially higher disease burden • Use of government RSV surveillance data may be helpful in decision-making
Discontinuation of Prophylaxis Among Children who Experience Breakthrough RSV Hospitalization
• Discontinue prophylaxis
Prophylaxis in the Second Year of Life
• Recommended in children who require ≥28 days of supplemental oxygen after birth and continue to require medical intervention (supplemental oxygen, chronic corticosteroid therapy, diuretics)
Number of Monthly Doses in Season

• Maximum of 5
Other
• Prophylaxis is not recommended for prevention of primary asthma or reduction of subsequent wheezing episodes • Prophylaxis is not recommended for prevention of nosocomial disease • Not recommended for use in RSV treatment

Because 5 monthly doses of Synagis will provide more than 6 months of adequate serum concentrations for most infants, administration should be limited to the peak RSV season in the continental United States of November through March. Qualifying infants born during RSV season will need fewer than 5 doses for protection until the season ends.

Specific information about national and regional RSV trends, especially pertaining to the peak variations in Florida and Alaska, is available from the National Respiratory and Enteric Virus Surveillance System (NREVSS) at: http://www.cdc.gov/surveillance/nrevss/rsv/index.html.

In February 2024, the AAP issued guidance for prevention of RSV disease to address the availability of Beyfortus for RSV prevention. Beyfortus is a single dose alternative to Synagis recommended for prevention in a broader population. AAP states that Beyfortus is preferred over Synagis because of its efficacy, duration and convenience.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Synagis (palivizumab)

Requests for Synagis (palivizumab) may be approved if the following criteria are met (2014 AAP, 2024 AAP):

I. Individual has not received Beyfortus (nirsevimab) for prevention of respiratory syncytial virus (RSV) lower respiratory tract disease for this RSV season; **AND**
II. Individual does not have access to Beyfortus (nirsevimab) for prevention of respiratory syncytial virus (RSV) lower respiratory tract disease; **AND**

III. A maximum of 5 doses of Synagis may be approved for **infants during the first RSV season within the first year of life** with any of the following:
    A. Born before 29 weeks, 0 days gestation (up to and including 28 weeks, 6 days) and younger than 12 months of age at the start of the RSV season; **OR**
    B. Documentation is provided indicating chronic lung disease of prematurity defined as birth at less than 32 weeks, 0 days gestation and a requirement for greater than 21% oxygen for at least 28 days after birth (not including asthma, reactive airway disease and cystic fibrosis without significant symptoms; **OR**
    C. Documentation is provided indicating hemodynamically significant congenital heart disease (including infants with acyanotic heart disease who are receiving medication to control congestive heart failure and will require cardiac surgical procedures and infants with moderate to severe pulmonary hypertension); **OR**
    D. Documentation is provided indicating anatomic pulmonary abnormalities (for example, tracheal ring) or a neuromuscular condition that impairs the ability to clear secretions from the upper airway because of ineffective cough; **OR**
    E. Documentation is provided indicating cystic fibrosis with clinical evidence of chronic lung disease or nutritional compromise (weight for length less than tenth percentile);

OR

IV. A maximum of 5 doses of Synagis may be approved for **children during their second RSV season** (the second RSV season may fall in the first or second year of life) with any of the following:
    A. Documentation is provided indicating the individual is a preterm infant born at less than 32 weeks, 0 days gestation who required at least 28 days of oxygen after birth AND continues to require medical intervention within 6 months of the start of the second RSV season (including supplemental oxygen, chronic systemic corticosteroid therapy or diuretics); **OR**

B. Documentation is provided indicating cystic fibrosis with severe lung disease (history of hospitalization, abnormal chest x-ray or CT scan) or weight for length less than tenth percentile;

OR

V. A maximum of 5 doses of Synagis may be approved for **children younger than 24 months of age** with any of the following:

A. Documentation is provided indicating profound immunocompromised status (such as severe combined immunodeficiency, advanced acquired immunodeficiency syndrome, undergoing organ or hematopoietic stem cell transplant, or an absolute lymphocyte count of less than 100 cells/mm^3); **OR**

B. Documentation is provided indicating the individual is undergoing cardiac transplantation;

OR

VI. One additional dose of Synagis may be approved for children younger than 24 months of age who have approval for a course of treatment and who undergo cardiopulmonary bypass for a surgical procedure.

*Synagis approval is limited to RSV season as determined by CDC surveillance data (http://www.cdc.gov/surveillance/nrevss/rsv/index.html) or local health department.
Up to 5 doses may be approved during the months of November through March.
Initiating therapy or providing additional doses for continued therapy in regions with high levels of interseasonal RSV activity may be approved on a case by case basis.

Synagis (palivizumab) may not be approved for any of the following:

I. Continued RSV prophylaxis for children who experience breakthrough RSV hospitalization; **OR**
II. Treatment of known RSV disease; **OR**
III. Children who reach 24 months of age prior to the beginning of RSV season; **OR**
IV. More than two seasons of RSV prophylaxis (unless individual is profoundly immunocompromised or undergoing cardiac transplantation); **OR**
V. Primary asthma prevention or to reduce subsequent episodes of wheezing; **OR**
VI. Children with surgically corrected congenital heart disease or hemodynamically insignificant heart disease (including secundum atrial septal defect, small ventricular septal defect, uncomplicated pulmonic stenosis, uncomplicated aortic stenosis, mild coarctation of the aorta, and patent ductus arteriosus) who do not otherwise meet approval criteria; **OR**
VII. Children with Down syndrome who do not otherwise meet approval criteria; **OR**
VIII. May not be approved when the above criteria are not met and for all other indications.

Quantity Limits

Synagis (palivizumab) Quantity Limit

Drug	Limit
Synagis (palivizumab) 50 mg, 100 mg vial	15 mg/kg once a month for up to 5 doses per RSV season
Override Criteria	
One additional dose may be approved for individuals undergoing cardiopulmonary bypass for a surgical procedure as noted in clinical criteria.	

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT

90378	Respiratory syncytial virus, monoclonal antibody, recombinant, for intramuscular use, 50 mg, each [Synagis]

HCPCS

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

ICD-10 Diagnosis

D81.0-D81.2	Severe Combined Immunodeficiency disorder [SCID]
D81.9	Severe Combined Immunodeficiency disorder, NOS
P07.21	Extreme immaturity of newborn, GA <23 completed weeks
P07.22	Extreme immaturity of newborn, GA 23 completed weeks
P07.23	Extreme immaturity of newborn, GA 24 completed weeks
P07.24	Extreme immaturity of newborn, GA 25 completed weeks
P07.25	Extreme immaturity of newborn, GA 26 completed weeks
P07.26	Extreme immaturity of newborn, GA 27 completed weeks
P07.31	Preterm newborn, GA 28 completed weeks
P07.32	Preterm newborn, GA 29 completed weeks
P07.33	Preterm newborn, GA 30 completed weeks
P07.34	Preterm newborn, GA 31 completed weeks
P07.35	Preterm newborn, GA 32 completed weeks
P07.36	Preterm newborn, GA 33 completed weeks*
P07.37	Preterm newborn, GA 34 completed weeks*
P07.38	Preterm newborn, GA 35 completed weeks*
P27.1	Bronchopulmonary dysplasia originating in the perinatal period
P27.8	Other chronic respiratory diseases originating in the perinatal period
P27.9	Unspecified chronic respiratory disease originating in the perinatal period
P29.30	Pulmonary hypertension of newborn
I42.9	Cardiomyopathy, unspecified
I50.9	Heart failure, unspecified
Q20.0	Common arterial trunk
Q20.1	Double outlet right ventricle
Q20.2	Double outlet left ventricle
Q20.3	Discordant ventriculoarterial connection
Q20.4	Double inlet ventricle
Q20.5	Discordant atrioventricular connection
Q20.6	Isomerism of atrial appendages
Q20.8	Other congenital malformations of cardiac chambers and connections
Q20.9	Congenital malformation of cardiac chambers and connections, unspecified
Q21.0	Ventricular septal defect
Q21.10-Q21.19	Atrial septal defect
Q21.20-Q21.23	Atrioventricular septal defect

Q21.3	Tetralogy of Fallot
Q21.4	Aortopulmonary septal defect
Q21.8	Other congenital malformations of cardiac septa
Q21.9	Congenital malformation of cardiac septum, unspecified
Q22.0	Pulmonary valve atresia

Document History

Revised: 8/16/2024
Document History:

- 8/16/2024 – Annual Review: Add criteria limiting use of Synagis to when Beyfortus is not accessible. Coding Reviewed: Added ICD-10-CM D81.0-D81.2, D81.9.
- 8/18/2023 – Annual Review: Add may not approve criteria for combination with Beyfortus. Coding Reviewed: No changes.
- 2/24/2023 – Select Review: Add clarification to address regions with high levels of interseasonal RSV activity. Add clarification of two season limitation. Coding Reviewed: Added ICD-10-CM Q21.10-Q21.19, Q21.20-Q21.23.
- 8/19/2022 – Annual Review: Remove note on delayed 2021 RSV season. Clarify Synagis season language. Wording and formatting changes. Coding Reviewed: Removed ICD-10-CM P07.21-P07.26, P07.31-P07.38, P27.8-P27.9, Q20.0-Q20.9, Q21.0-Q21.8. Added ICD-10-CM P07.21, P07.22, P07.23, P07.24, P07.25, P07.26, P07.31, P07.32, P07.33, P07.34, P07.35, P07.36, P07.37, P07.38, P27.8, P27.9, P29.30, Q20.0, Q20.1, Q20.2, Q20.3, Q20.4, Q20.5, Q20.6, Q20.8, Q20.9, Q21.0, Q21.1, Q21.2, Q21.3, Q21.4, Q21.8, Q21.9.
- 12/20/2021 – Minor wording change.
- 10/07/2021 – Minor adjustments on seasonality.
- 8/20/2021 – Annual Review: Add note providing direction on how to address the delayed 2021 RSV season and to refer to CDC website for RSV season by region. Add exclusion for more than two seasons of prophylaxis. Wording and formatting changes. Coding reviewed: Added ICD-10-CM P07.21-P07.26, P07.31-P07.38, P27.1, P27.8-P27.9, I42.9, I50.9, Q20.0-Q20.9, Q21.0-Q21.8, Q22.0
- 11/30/2020 – Administrative update to add documentation requirements.
- 8/21/2020 – Annual Review: No changes. Coding Reviewed: No changes.
- 09/23/2019 – Administrative update to add drug specific quantity limit.
- 09/09/2019 - Annual Review: Wording and formatting changes. Coding reviewed: No changes.
- 08/17/2018 – Annual Review: Wording and formatting updates. Add in reference for criteria.

References

1. AAP Recommendations for the Prevention of RSV Disease in Infants and Children. Red Book Online. February 21, 2024. Available at https://publications.aap.org/redbook/resources/25379. Accessed: July 11, 2024.
2. 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. Last 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: July 11, 2024.
3. American Academy of Pediatrics Committee on Infectious Diseases and Bronchiolitis Guidelines Committee. Updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection: Policy Statement. *Pediatrics*. 2014; 134(2):415-420. Erratum in: Pediatrics. 2014; 134(6):1221. Available at: http://pediatrics.aappublications.org/content/134/2/415.full. Accessed: July 11, 2024.
4. American Academy of Pediatrics Committee on Infectious Diseases and Bronchiolitis Guidelines Committee. Updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection: Technical Report. *Pediatrics*. 2014; 134(2):e620-e638. Available at: http://pediatrics.aappublications.org/content/134/2/e620.full.pdf+html. Accessed: July 11, 2024.
5. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: July 7, 2024.
6. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
7. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.