

Reference number
1988-A

SPECIALTY GUIDELINE MANAGEMENT

SYNAGIS (palivizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Synagis is indicated for the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus (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 (CHD) and who are 24 months of age or younger at the beginning of RSV season

Limitations of Use:

The safety and efficacy of Synagis have not been established for treatment of RSV disease.

B. Compendial Uses

1. RSV prophylaxis in infants with congenital abnormalities of the airway or neuromuscular disease that compromise handling of respiratory secretions
2. RSV prophylaxis in immunocompromised pediatric patients
3. RSV prophylaxis in pediatric patients with cystic fibrosis who have evidence of chronic lung disease or nutritional compromise in the first year of life

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of up to 5 doses per RSV season may be granted for the prevention of serious lower respiratory tract disease caused by RSV when a member has any of the following diagnoses and meets the criteria pertaining to the diagnosis:

1. Prematurity
2. Chronic lung disease (CLD) of prematurity
3. Congenital heart disease (CHD) (See Appendix B)
4. Congenital airway abnormality
5. Neuromuscular condition
6. Immunocompromised children
7. Cystic fibrosis

A. Prematurity

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All of the following criteria are met:

1. Member's gestational age is < 29 weeks, 0 days.
2. Member's chronological age at the start of RSV season is < 12 months.

B. CLD of prematurity

ALL of the following criteria must be met:

1. Member's gestational age is < 32 weeks, 0 days.
2. Requirement for > 21% oxygen for at least the first 28 days after birth.
3. Member meets either of the following criteria:
 - i. Member's chronological age at the start of their first RSV season is < 12 months.
 - ii. Member's chronological age at the start of the subsequent RSV season is < 24 months and the member continues to require medical support (e.g., chronic corticosteroids, diuretic therapy, supplemental oxygen) during the 6-month period prior to the start of the RSV season.

C. CHD

All of the following criteria are met:

1. CHD is hemodynamically significant.
2. Member meets either of the following criteria:
 - i. Member's chronological age at the start of RSV season is < 12 months.
 - ii. Member's chronological age at the start of RSV season is between 12 to 24 months and the member will be undergoing cardiac transplantation during the RSV season.

D. Congenital airway abnormality

All of the following criteria must be met:

1. The condition compromises handling of respiratory secretions.
2. Member's chronological age at the start of RSV season is < 12 months.

E. Neuromuscular condition

All of the following criteria must be met:

1. The condition compromises handling of respiratory secretions.
2. Member's chronological age at the start of RSV season is < 12 months.

F. Immunocompromised children

All of the following criteria must be met:

1. Member is profoundly immunocompromised during the RSV season (e.g., SCID, stem cell transplant, bone marrow transplant)
2. Member's chronological age at the start of the RSV season is <24 months

G. Cystic Fibrosis

Either of the following criteria must be met:

1. Member's chronological age at the start of the RSV season is < 12 months and the member has evidence of CLD or nutritional compromise
2. Member's chronological age at the start of RSV season is between 12 to 24 months and the member has manifestations of lung disease (e.g., hospitalizations for pulmonary exacerbations) or weight for length less than the 10th percentile

III. 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 $\geq 10\%$ (with rapid antigen testing) or $\geq 3\%$ (with real-time polymerase chain reaction (PCR) test) within 2 weeks of the intended dose according to the

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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 or state (<http://www.cdc.gov/surveillance/nrevss/rsv/index.html>). Other Specialty Guideline Management criteria apply.

CVS Caremark PBM Synagis Season will be from November 1st to March 31st. Other health plans may differ. For the current 2021-2022 fall and winter season, the American Academy of Pediatrics (AAP) recommends beginning administration of Synagis prophylaxis in all regions of the country at the usual time, regardless of whether or not an area experienced unusual interseasonal RSV activity (i.e., increased activity in the spring and summer of 2021). Please note, any doses received prior to November 1st will not count towards the 2021-2022 season's 5 dose total.

IV. APPENDIX

Appendix A: Recommended Use of Synagis for Prevention of RSV Infection

Recommendations from the American Academy of Pediatrics for the prevention of RSV infection with Synagis are summarized in Table below. 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.

Table. Recommended Use of Synagis for Prevention of RSV Infection

Prematurity	<ul style="list-style-type: none"> • Preterm infants born < 29 weeks, 0 days of gestation who are younger than 12 months at the start of the RSV season
Congenital Heart Disease	<ul style="list-style-type: none"> • Infants and children < 12 months of age with hemodynamically significant CHD • Those most likely to benefit from prophylaxis include: <ul style="list-style-type: none"> ○ Infants with acyanotic heart disease who are receiving medication to control congestive heart failure and will require cardiac surgical procedures ○ Infants with moderate to severe pulmonary hypertension • Infants and children < 24 months of age who undergo cardiac transplantation during the RSV season
Chronic Lung Disease of Prematurity	<ul style="list-style-type: none"> • For the first RSV season during the first year of life: Preterm infants who develop CLD of prematurity defined as: <ul style="list-style-type: none"> ○ Gestational age < 32 weeks, 0 days <u>AND</u> ○ Requirement for > 21% oxygen for at least the first 28 days after birth • For the second RSV season during the second year of life: Preterm infants who: <ul style="list-style-type: none"> ○ Satisfy the above definition of CLD of prematurity <u>AND</u> ○ Continue to require medical support* for CLD during the 6-month period prior to the start of the second RSV season

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Congenital Abnormality of the Airway/ Neuromuscular Condition	<ul style="list-style-type: none"> • Infants who have either a significant congenital abnormality of the airway or a neuromuscular condition that compromises handling of respiratory secretions for the first year of life
Immunocompromised children	<ul style="list-style-type: none"> • Children younger than 24 months of age who are profoundly immunocompromised during the RSV season
Cystic Fibrosis	<ul style="list-style-type: none"> • For the first year of life, children with clinical evidence of CLD and/or nutritional compromise • For the second year of life, children with manifestations of severe lung disease (previous hospitalization for pulmonary exacerbation in the first year of life or abnormalities on chest radiography or chest computed tomography that persist when stable) OR weight for length less than the 10th percentile.

Abbreviations: CHD = congenital heart disease; CLD = chronic lung disease (formerly bronchopulmonary dysplasia); RSV = respiratory syncytial virus.

* Medical support includes supplemental oxygen, diuretic therapy, or chronic corticosteroid therapy.

Appendix B: Examples of Congenital Heart Anomalies*

- Atrial or ventricular septal defect
- Patent ductus arteriosus
- Coarctation of aorta
- Tetralogy of Fallot
- Pulmonary or aortic valve stenosis
- D-Transposition of great arteries
- Hypoplastic left/right ventricle
- Truncus arteriosus
- Total anomalous pulmonary venous return
- Tricuspid atresia
- Ebstein's anomaly
- Pulmonary atresia
- Single ventricle
- Double-outlet right ventricle

*Must be hemodynamically significant. See Table above for examples of infants and children who are most likely to benefit from Synagis.

V. REFERENCES

1. Synagis [package insert]. Gaithersburg, MD: MedImmune, LLC; May 2017.
2. American Academy of Pediatrics. Updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection. *Pediatrics*. 2014;134(2):415-20.
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: <https://dx.doi.org/10.15585/mmwr.mm6702a4>. Accessed May 20, 2020.

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4. Bernstein D. Epidemiology and Genetic Basis of Congenital Heart Disease. In: Kliegman RM, St. Geme J. Nelson Textbook of Pediatrics, Edition 21. Chap. 451. Philadelphia, PA: Elsevier; 2020. Accessed May 26, 2020.
5. Midgley CM, Haynes AK, Baumgardner JL, et.al. Determining the Seasonality of Respiratory Syncytial Virus in the United States: The Impact of Increased Molecular Testing. *The Journal of Infectious Disease*. 1 August 2017; 216(3): 345-355.
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. <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 4, 2022.