SYNAGIS®
PALIVIZUMAB

25+ YEARS OF CLINICAL EXPERIENCE
PROTECTING THE HIGHEST RISK INFANTS FROM RSV

SYNAGIS® (palivizumab): Over 25 Years of Real-World Use for the Prevention of Severe RSV Disease[1]

- SYNAGIS is the first FDA-approved monoclonal antibody for prophylaxis to help prevent RSV in high-risk infants and children.[1]
- The efficacy and safety of SYNAGIS were clinically established in premature infants with and without BPD and children aged ≤24 months with hemodynamically significant CHD.[1]

For over 25 years, high-risk infants have been treated with SYNAGIS to help reduce the risk of RSV-related hospitalizations.[1]

SYNAGIS is not a vaccine.[1,2,*]

BPD=bronchopulmonary dysplasia; CHD=congenital heart disease; FDA=US Food and Drug Administration; RSV=respiratory syncytial virus.

*Unlike vaccines, antibodies do not provide long-lasting immunity. SYNAGIS needs to be given each month (every 28 to 30 days) throughout the RSV season to provide continuous protection against RSV.[1,2]

INDICATION

SYNAGIS, 50 mg and 100 mg for injection, 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 (≤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.

CONTRAINDICATIONS

Previous significant hypersensitivity reaction to SYNAGIS.

IMPORTANT SAFETY INFORMATION

Hypersensitivity Reactions: Anaphylaxis and anaphylactic shock (including fatal cases) and other severe acute hypersensitivity reactions have been reported. Permanently discontinue SYNAGIS and administer appropriate medication if such reactions occur.

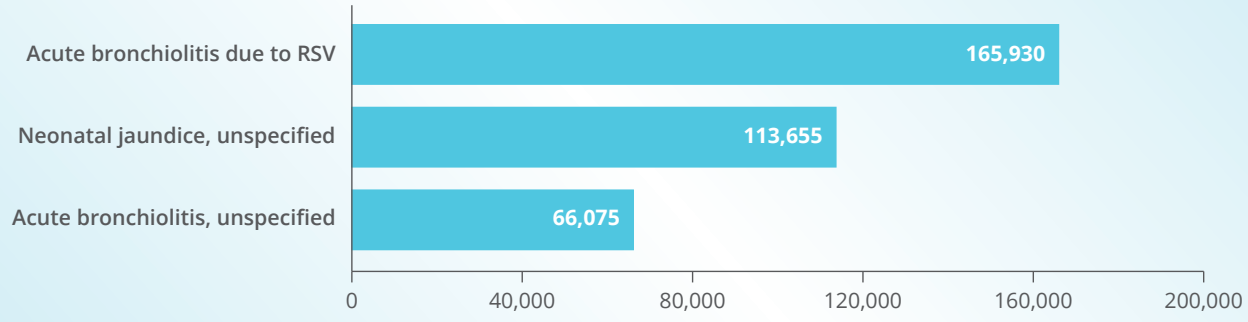
Please see additional Important Safety Information throughout and on page 9.
Please click here for full Prescribing Information for SYNAGIS, including Patient Information.

Severe RSV Disease Has Healthcare Resource Utilization and Economic Implications

Severe RSV disease is the leading cause of hospitalization in infants aged <1 year in the United States[3]

A retrospective study of the National Inpatient Sample between 2009 and 2019 found that acute bronchiolitis due to RSV was the most frequent primary diagnosis for infants aged <1 year. The following chart shows the top hospitalization causes for infants between 2015 and 2019.[3]

Total Infant (<1 Year) Hospitalizations (2015-2019)[3]



- Another study showed that **hospitalization rates for severe RSV disease were ~13x higher** than those for influenza in infants aged <1 year.[4]
- A retrospective, observational cohort study using MarketScan Commercial and Multi-State Medicaid administrative claims databases found that[5]
  - RSV hospitalization rates for very preterm infants (<29 wGA) with commercial coverage have **increased from 1.0 per 100** infant seasons in 2004-2005 **to 4.4 per 100** infant seasons in 2019-2020.
  - Very preterm infants (<29 wGA) with **commercial** coverage were **nearly 3x more likely** to be hospitalized for RSV in the first year of life than term infants.
  - Very preterm infants (<29 wGA) with **Medicaid** coverage were **more than 3.5x more likely** to be hospitalized for RSV in the first year of life than term infants.

wGA=weeks gestational age.

IMPORTANT SAFETY INFORMATION (cont'd)

Coagulation Disorders: SYNAGIS should be given with caution to children with thrombocytopenia or any coagulation disorder.

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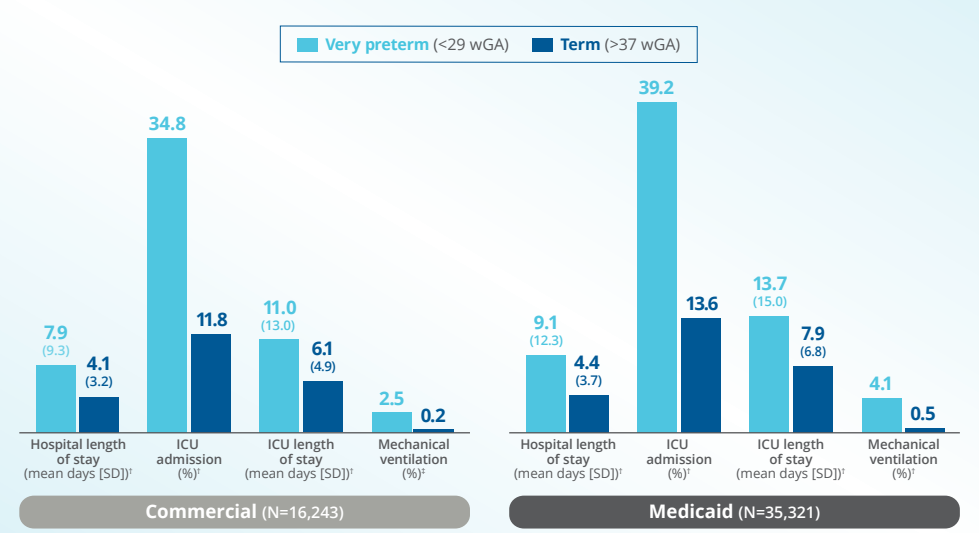
Severe RSV Disease Has Healthcare Resource Utilization and Economic Implications (cont'd)

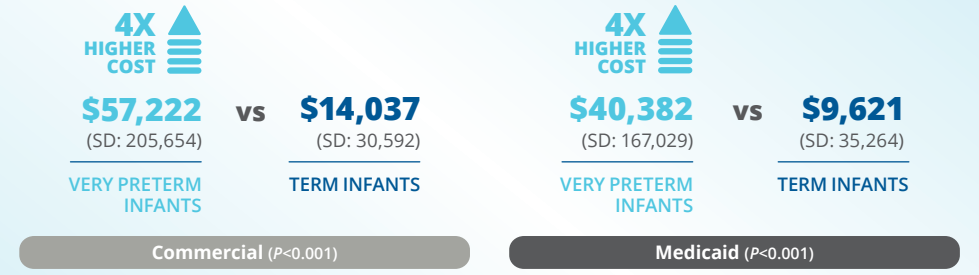
In a real-world study, very preterm infants (<29 wGA) had greater RSV hospitalization-related severity compared with term infants[5]

A real-world study* comparing RSV hospitalization and RSV hospitalization characteristics in medically fragile, very preterm infants (<29 wGA) and term infants (>37 wGA) during the 2003 through 2020 RSV seasons found that hospital length of stay, ICU admission and length of stay, invasive mechanical ventilation, and the average cost of RSV hospitalization was higher for very preterm infants than term infants.[5]

RSV Hospitalization Characteristics of Very Preterm (<29 wGA) and Term Infants (>37 wGA) by Payer[5]



Average Cost of RSV Hospitalization Was More Than 4x Higher for Very Preterm Infants vs Term Infants[5]



Medicaid costs are typically lower than commercial costs because Medicaid pays a negotiated rate that is required by law to be at or below the lowest price paid for a drug in the United States.

ICU=intensive care unit; SD=standard deviation.

*__Study design:__ In a retrospective, observational cohort study using the MarketScan Commercial and Multi-State Medicaid administrative claims databases, infants born between July 1, 2003 and June 30, 2020 were identified and classified as very preterm (N=40,123) or term (N=4,421,942). Infants with evidence of health conditions, such as CHD and cystic fibrosis, were excluded. During the 2003 through 2020 RSV seasons (November to March), claims incurred by infants while they were <12 months old were evaluated for outpatient administration of SYNAGIS® (palivizumab) and RSV hospitalization.[5]

__Primary objective:__ To characterize outpatient SYNAGIS prophylaxis and risk of RSV hospitalization among very preterm infants and to compare the course of RSV hospitalization among these infants.[5]

__Study limitations:__ This study used retrospectively collected administrative claims data, which could contain coding errors and omission of unbilled or over-the-counter services. Data on inpatient administration of SYNAGIS was not available in the database; only outpatient administrations were measured. Some infants in the subgroup without outpatient SYNAGIS use may have received SYNAGIS during the birth hospitalization or a subsequent hospitalization, possibly resulting in misclassification error. RSV hospitalization may have occurred in some infants prior to SYNAGIS administration. In addition, infants with a single outpatient dose of SYNAGIS were included, although the recommended dosing interval is monthly. The study was restricted to commercially insured and Medicaid-insured infants.[5]

†*P*<0.001 vs term infants.[5]

‡*P*=0.007.[5]

IMPORTANT SAFETY INFORMATION (cont'd)

RSV Diagnostic Test Interference: Palivizumab may interfere with immunological-based RSV diagnostic tests, such as some antigen detection-based assays.

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Severe RSV Disease Has Healthcare Resource Utilization and Economic Implications (cont'd)

Children with BPD aged <24 months have a greater risk of RSV-related hospitalization compared with term infants[6,*]

Children with BPD aged <24 months had **up to a 20x greater rate** of RSV-related hospitalizations vs term infants[6]

Infants aged <6 months had

~13x greater rate

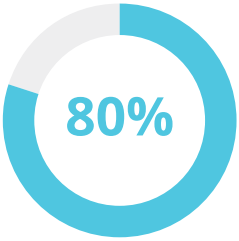
Infants aged 6 months to <12 months had

~14x greater rate

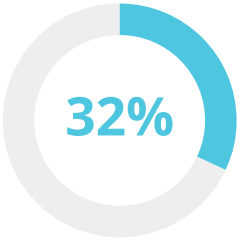
Children aged 12 months to <24 months had

~20x greater rate

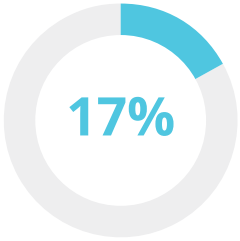
Once hospitalized, children with BPD/CLDP ≤24 months are at an increased risk of needing **oxygen supplementation, intensive care, and invasive mechanical ventilation**. Among 200 children with CLD hospitalized with RSV infection[7,†]:



required oxygen supplementation



required intensive care



required invasive mechanical ventilation

*Based on a retrospective study analyzing hospitalizations for RSV-related illness in children aged <3 years enrolled in the Tennessee Medicaid system between July 1989 and June 1993. Rates are based on expected hospitalizations per year per 1000 children.[6]

†Based on a retrospective chart review of morbidity and mortality among patients identified with RSV by viral isolation or antigen detection at 12 tertiary care pediatric centers from 1988 to 1991. Children (N=1584) were included if they had lower respiratory tract infection and at least 1 of the following: CHD, CLD, immunosuppression, prematurity (<36 wGA), age <6 weeks, and oxygen saturation <90% or arterial oxygen pressure <60 mm Hg in room air.[7]

CLD=chronic lung disease; CLDP=chronic lung disease of prematurity.

IMPORTANT SAFETY INFORMATION (cont'd)

Serious Adverse Reactions: The most common serious adverse reactions occurring with SYNAGIS are anaphylaxis and other acute hypersensitivity reactions.

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The Virology of RSV Has Changed Since COVID-19, Adding to the Clinical and Economic Burden

Prior to COVID-19, RSV was typically seasonal, varying by year and geographic location, with most of the United States experiencing a rise in RSV cases in the fall lasting through the spring.[8,9]

Masking, social distancing, and changes in viral interactivity since the COVID-19 pandemic have **altered RSV epidemiology**.[8,9]

Due to these variables, **the seasonal nature of RSV is no longer clear-cut**, and according to the CDC, it is still **too soon** to predict when the previous seasonal patterns will return.[8,9]

These circumstances have led the AAP to recommend the use of SYNAGIS® (palivizumab) in eligible infants throughout the period of widespread and intense RSV circulation, even if disease activity lasts longer than the typical duration.[8]

Help protect your high-risk members by allowing open access to SYNAGIS throughout the year.

"Given this information, together with the known efficacy of palivizumab and unpredictable epidemiology of RSV since the summer of 2021, the AAP recommends programmatic consideration of providing more than 5 consecutive doses* of palivizumab depending on the duration of the current RSV surge in a given region of the country."

— Updated AAP Guidance, November 2022[8]

*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. Children who develop an RSV infection should continue to receive monthly doses throughout the RSV season.[1]

AAP=American Academy of Pediatrics; CDC=Centers for Disease Control and Prevention.

IMPORTANT SAFETY INFORMATION (cont'd)

Most Common Adverse Reactions: The most common adverse reactions are fever and rash.

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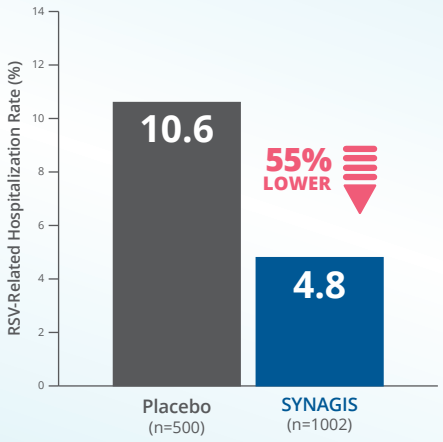
SYNAGIS® (palivizumab) Has Been Proven to Reduce RSV-Related Hospitalization

In preterm infants with and without BPD, SYNAGIS significantly reduced RSV hospitalization by 55% vs placebo[10,*]

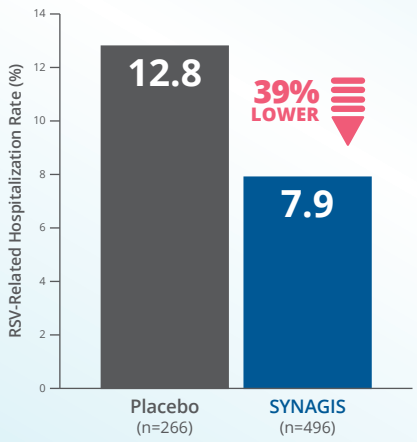
Primary Endpoint[10]

All Subjects (*P*<0.001)

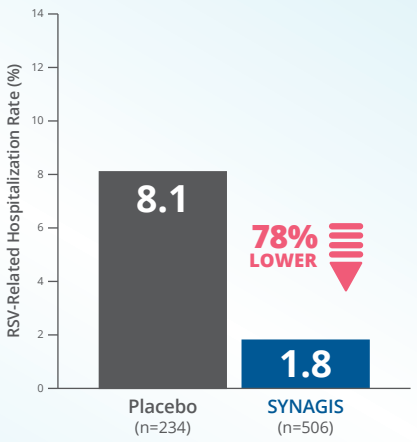


Subgroup Analysis[10]

Infants With BPD (*P*=0.038)



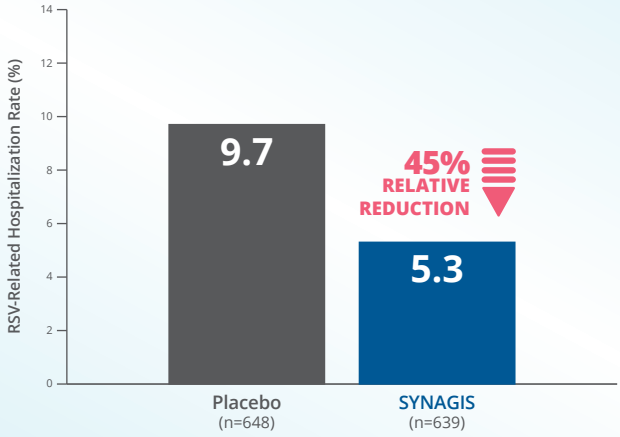
Infants Without BPD (*P*<0.001)



In children with CHD, SYNAGIS reduced RSV hospitalization by nearly half vs placebo[11,†]

Significant Reduction in RSV-Related Hospitalization Rates With SYNAGIS[11]

Children Aged ≤24 Months (*P*=0.003)



*Based on the IMpact-RSV Study, a multicenter, randomized, double-blind, placebo-controlled study conducted at 139 centers in the United States, United Kingdom, and Canada in 1502 children who were either ≤35 wGA and aged ≤6 months or ≤24 months with a clinical diagnosis of BPD requiring ongoing treatment in the past 6 months.[10]

†Based on a multicenter, randomized, double-blind, placebo-controlled trial in 1287 children aged ≤24 months with CHD during 4 consecutive RSV seasons from 1998 through 2002.[11]

IMPORTANT SAFETY INFORMATION (cont'd)

Postmarketing Experience: Severe thrombocytopenia and injection site reactions have been identified during post approval use of SYNAGIS.

Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

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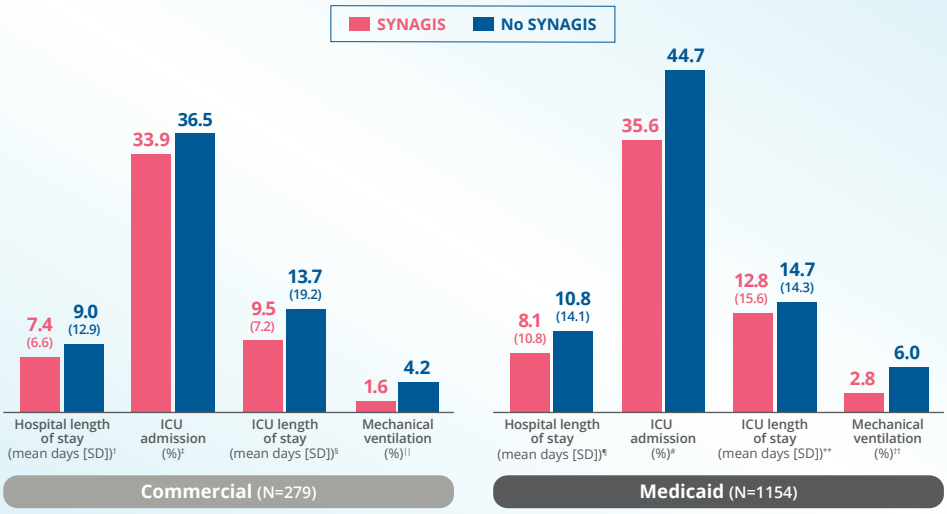
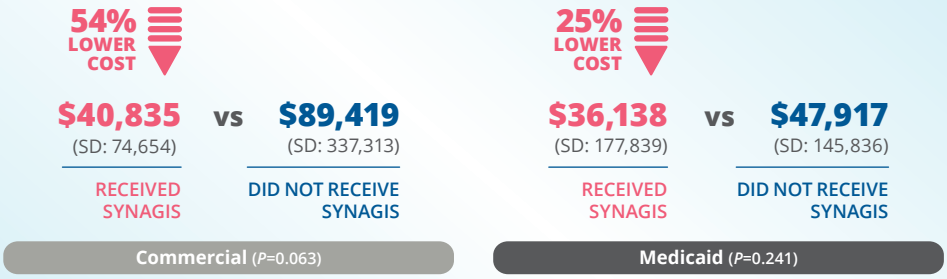
SYNAGIS® (palivizumab) Has Been Proven to Reduce RSV-Related Hospitalization Severity and Costs

In a real-world study,* RSV-related hospitalization costs and severity were reduced among very preterm infants who received SYNAGIS in an outpatient setting[5]

RSV Hospitalization Characteristics of Very Preterm Infants (<29 wGA) by SYNAGIS Use and Payer[5]



Average Cost of RSV Hospitalization Was Lower for Very Preterm Infants Who Received SYNAGIS[5]



Medicaid costs are typically lower than commercial costs because Medicaid pays a negotiated rate that is required by law to be at or below the lowest price paid for a drug in the United States.

Less than 60% of very preterm infants received outpatient SYNAGIS prophylaxis, resulting in suboptimal protection against severe RSV.[5]

*__Study design:__ In a retrospective, observational cohort study using the MarketScan Commercial and Multi-State Medicaid administrative claims databases, infants born between July 1, 2003 and June 30, 2020 were identified and classified as very preterm (N=40,123) or term (N=4,421,942). Infants with evidence of health conditions, such as CHD and cystic fibrosis, were excluded. During the 2003 through 2020 RSV seasons (November to March), claims incurred by infants while they were <12 months old were evaluated for outpatient administration of SYNAGIS and RSV hospitalization.[5]

__Primary objective:__ To characterize outpatient SYNAGIS prophylaxis and risk of RSV hospitalization among very preterm infants and to compare the course of RSV hospitalization among these infants.[5]

__Study limitations:__ This study used retrospectively collected administrative claims data, which could contain coding errors and omission of unbilled or over-the-counter services. Data on inpatient administration of SYNAGIS was not available in the database; only outpatient administrations were measured. Some infants in the subgroup without outpatient SYNAGIS use may have received SYNAGIS during the birth hospitalization or a subsequent hospitalization, possibly resulting in misclassification error. RSV hospitalization may have occurred in some infants prior to SYNAGIS administration. In addition, infants with a single outpatient dose of SYNAGIS were included, although the recommended dosing interval is monthly. The study was restricted to commercially insured and Medicaid-insured infants.[5]

†$P<0.001$ vs infants who received SYNAGIS.[5]
‡$P=0.667$.[5]
§$P=0.008$.[5]
‖$P=0.200$.[5]
¶$P=0.019$.[5]
#$P=0.002$.[5]
**$P=0.191$.[5]
††$P=0.007$.[5]

IMPORTANT SAFETY INFORMATION (cont'd)

Hypersensitivity Reactions: Anaphylaxis and anaphylactic shock (including fatal cases) and other severe acute hypersensitivity reactions have been reported. Permanently discontinue SYNAGIS and administer appropriate medication if such reactions occur.

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SYNAGIS® (palivizumab)— Over 25 Years of Real-Word Evidence

Proven protection against severe RSV disease[1]

- **Delivers immediately available RSV-blocking antibodies** and monthly weight-tailored dosing for eligible high-risk infants[1]
- Is **not a vaccine**[1,2]
  - Unlike vaccines, antibodies do not provide long-lasting immunity. SYNAGIS needs to be given each month (every 28 to 30 days) throughout the RSV season to provide continuous protection against RSV.

According to the CDC, RSV seasons have not been consistent since the start of the COVID-19 pandemic in early 2020, and it is too soon to predict when those seasonal patterns may return.[9]

Help protect your high-risk members by allowing open access to SYNAGIS throughout the year.

IMPORTANT SAFETY INFORMATION (cont'd)

Coagulation Disorders: SYNAGIS should be given with caution to children with thrombocytopenia or any coagulation disorder.

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IMPORTANT PRODUCT INFORMATION

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LIMITATIONS OF USE

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CONTRAINDICATIONS

Previous significant hypersensitivity reaction to SYNAGIS.

IMPORTANT SAFETY INFORMATION

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RSV Diagnostic Test Interference: Palivizumab may interfere with immunological-based RSV diagnostic tests, such as some antigen detection-based assays.

Serious Adverse Reactions: The most common serious adverse reactions occurring with SYNAGIS are anaphylaxis and other acute hypersensitivity reactions.

Most Common Adverse Reactions: The most common adverse reactions are fever and rash.

Postmarketing Experience: Severe thrombocytopenia and injection site reactions have been identified during post approval use of SYNAGIS.

Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

These are not all the possible risks associated with SYNAGIS.

Please click here for full Prescribing Information for SYNAGIS, including Patient Information.

To report suspected adverse reactions, contact Sobi North America at 1-866-773-5274 or the FDA at 1-800-FDA-1088.

References: 1. SYNAGIS (palivizumab) [prescribing information]. Waltham, MA: Sobi, Inc; 2021. **2.** Delves PJ, Martin SJ, Burton DR, Roitt IM. Vaccines. *Roitt's Essential Immunology*. 11th ed. Malden, MA: Blackwell Publishing; 2006:287-311. **3.** Suh M, Movva N, Jiang X, et al. Respiratory syncytial virus is the leading cause of United States infant hospitalizations, 2009-2019: a study of the National (Nationwide) Inpatient Sample. *J Infect Dis.* 2022;226(suppl 2):S154-S163. doi:10.1093/infdis/jiac120 **4.** Goldstein E, Finelli L, O'Halloran A, et al. Hospitalizations associated with respiratory syncytial virus (RSV) and influenza in children, including children diagnosed with asthma. *Epidemiology*. 2019;30(6):918-926. doi:10.1097/EDE.0000000000001092 **5.** Packnett ER, Winer IH, Larkin H, et al. RSV-related hospitalization and outpatient palivizumab use in very preterm (born at <29 wGA) infants: 2003-2020. *Hum Vaccin Immunother.* 2022;18(6):e2140533. doi:10.1080/21645515.2022.2140533 **6.** Boyce TG, Mellen BG, Mitchel EF Jr, Wright PF, Griffin MR. Rates of hospitalization for respiratory syncytial virus infection among children in Medicaid. *J Pediatr.* 2000;137(6):865-870. doi:10.1067/mpd.2000.110531 **7.** Navas L, Wang E, de Carvalho V, Robinson J; on behalf of the Pediatric Investigators Collaborative Network on Infections in Canada. Improved outcome of respiratory syncytial virus infection in a high-risk hospitalized population of Canadian children. *Pediatrics.* 1992;121(3):348-354. doi:10.1016/s0022-3476(05)90000-0 **8.** Updated guidance: use of palivizumab prophylaxis to prevent hospitalization from severe respiratory syncytial virus infection during the 2022-2023 RSV season. American Academy of Pediatrics website. Updated November 17, 2022. Accessed May 11, 2023. https://www.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/interim-guidance-for-use-of-palivizumab-prophylaxis-to-prevent-hospitalization/ **9.** RSV surveillance & research. Centers for Disease Control and Prevention website. Reviewed October 28, 2022. Accessed May 11, 2023. https://www.cdc.gov/rsv/research/index.html **10.** The IMpact-RSV Study Group. Palivizumab, a humanized respiratory syncytial virus monoclonal antibody, reduces hospitalization from respiratory syncytial virus infection in high-risk infants. *Pediatrics.* 1998;102(3):531-537. **11.** Feltes TF, Cabalka AK, Meissner HC, et al; for the Cardiac Synagis Study Group. Palivizumab prophylaxis reduces hospitalization due to respiratory syncytial virus in young children with hemodynamically significant congenital heart disease. *J Pediatr.* 2003;143(4):532-540. doi:10.1067/s0022-3476(03)00454-2

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