Among infants <1 year old
RESPIRATORY SYNCYTIAL VIRUS (RSV) IS A LEADING CAUSE OF HOSPITALIZATION IN THE US

Help protect your vulnerable baby from severe RSV disease with SYNAGIS

RSV is a seasonal virus, like the flu, that is easily spread. Most children get RSV by age 2.

Ask your baby's doctor about SYNAGIS, an injection of virus-fighting antibodies given monthly during the RSV season.*

SYNAGIS®
PALIVIZUMAB

PROTECT WHAT MATTERS MOST

SYNAGIS—20+ YEARS OF HELPING TO PROTECT VULNERABLE BABIES FROM RSV

IMPORTANT SAFETY INFORMATION

Who should not receive SYNAGIS?

Children should not receive SYNAGIS if they have ever had a severe allergic reaction to it. Signs and symptoms of a severe allergic reaction could include itchy rash; swelling of the face; difficulty swallowing; difficulty breathing; bluish color of the skin; muscle weakness or floppiness; and/or unresponsiveness. If your child has any of these signs or symptoms of a severe allergic reaction after getting SYNAGIS, call your child's healthcare provider or get medical help right away.

How is SYNAGIS given?

SYNAGIS is given as a monthly injection, usually in the thigh (leg) muscle, by your child's healthcare provider. If your child has a problem with bleeding or bruises easily, an injection could cause a problem. Your child should receive their first injection of SYNAGIS before the RSV season starts, to help protect them before RSV becomes active. RSV season is usually fall through spring, but it may begin earlier or last longer in certain areas. When RSV is most active, your child will need to receive injections of SYNAGIS every 28-30 days to help protect them from severe RSV disease for about a month. Your child should continue to receive monthly injections of SYNAGIS until the end of RSV season. Your child may still get severe RSV disease after receiving SYNAGIS. If your child has an RSV infection, they should continue to get their monthly injections throughout the RSV season to help prevent severe disease from new RSV infections.

The effectiveness of injections of SYNAGIS given less than monthly throughout the RSV season has not been established.

What are the possible side effects of SYNAGIS?

Serious side effects include severe allergic reactions, which may happen after any injection of SYNAGIS and may be life-threatening or cause death. Call your child's healthcare provider or get medical help right away if your child has any of the signs or symptoms of a serious allergic reaction. See "Who should not receive SYNAGIS?" for more information.

Common side effects of SYNAGIS include fever and rash.

These are not all the possible side effects of SYNAGIS.

APPROVED USE

SYNAGIS, 50 mg and 100 mg for injection, is a prescription medication that is used to help prevent a serious lung disease caused by respiratory syncytial virus (RSV) in children:

- born prematurely (at or before 35 weeks) **and** who are 6 months of age or less at the beginning of RSV season
- who have a chronic lung condition called bronchopulmonary dysplasia (BPD), that needed medical treatment within the last 6 months, **and** who are 24 months of age or less at the beginning of RSV season
- born with certain types of heart disease **and** who are 24 months of age or less at the beginning of RSV season

It is not known if SYNAGIS is safe and effective:

- to *treat* the symptoms of RSV in a child who already has RSV. SYNAGIS is used to help *prevent* RSV disease
- in children who are older than 24 months of age at the start of dosing

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit **www.FDA.gov/medwatch** or call 1-800-FDA-1088.

*RSV season typically lasts 5 months in the United States; however, it can vary by year and geographic region. High-risk infants should receive monthly doses (every 28-30 days) throughout RSV season.

All imagery is for illustrative purposes only.

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Please see Brief Summary of Prescribing Information on adjacent page.

SYNAGIS®

(palivizumab) injection, for intramuscular use

BRIEF SUMMARY of PRESCRIBING INFORMATION.

For complete prescribing information consult official package insert.

INDICATIONS AND USAGE

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 *[see Clinical Studies (14) in full Prescribing Information].*

Limitations of Use:

The safety and efficacy of Synagis have not been established for treatment of RSV disease *[see Warnings and Precautions (5.4) in full Prescribing Information].*

DOSAGE AND ADMINISTRATION

Dosing Information

The recommended dose of Synagis is 15 mg per kg of body weight given monthly by intramuscular injection. 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. In the northern hemisphere, the RSV season typically commences in November and lasts through April, but it may begin earlier or persist later in certain communities.

Synagis serum levels are decreased after cardio-pulmonary bypass *[see Clinical Pharmacology (12.3) in full Prescribing Information].* Children undergoing cardio-pulmonary bypass should receive an additional dose of Synagis as soon as possible after the cardio-pulmonary bypass procedure (even if sooner than a month from the previous dose). Thereafter, doses should be administered monthly as scheduled.

The efficacy of Synagis at doses less than 15 mg per kg, or of dosing less frequently than monthly throughout the RSV season, has not been established.

Administration Instructions

- **DO NOT DILUTE THE PRODUCT.**
- **DO NOT SHAKE OR VIGOROUSLY AGITATE THE VIAL.**
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. Do not use any vials exhibiting particulate matter or discoloration.
- Using aseptic techniques, attach a sterile needle to a sterile syringe. Remove the flip top from the Synagis vial and wipe the rubber stopper with a disinfectant (e.g., 70% isopropyl alcohol). Insert the needle into the vial and withdraw into the syringe an appropriate volume of solution. Administer immediately after drawing the dose into the syringe.
- Synagis should be administered in a dose of 15 mg per kg intramuscularly using aseptic technique, preferably in the anterolateral aspect of the thigh. The gluteal muscle should not be used routinely as an injection site because of the risk of damage to the sciatic nerve. The dose (volume of injection in mL) per month = patient weight (kg) x 15 mg per kg ÷ 100 mg per mL of Synagis. Injection volumes over 1 mL should be given as a divided dose.
- Synagis is supplied as a single-dose vial and does not contain preservatives. Do not re-enter the vial after withdrawal of drug; discard unused portion. Only administer one dose per vial.
- Use sterile disposable syringes and needles. To prevent the transmission of hepatitis viruses or other infectious agents from one person to another, DO NOT reuse syringes and needles.

CONTRAINDICATIONS

Synagis is contraindicated in children who have had a previous significant hypersensitivity reaction to Synagis *[see Warnings and Precautions (5.1) in full Prescribing Information].*

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

Cases of anaphylaxis and anaphylactic shock, including fatal cases, have been reported following initial exposure or re-exposure to Synagis. Other acute hypersensitivity reactions, which may be severe, have also been reported on initial exposure or re-exposure to Synagis. Signs and symptoms may include urticaria, pruritus, angioedema, dyspnea, respiratory failure, cyanosis, hypotonia, hypotension, and unresponsiveness. The relationship between these reactions and the development of antibodies to Synagis is unknown. If a significant hypersensitivity reaction occurs with Synagis, its use should be permanently discontinued. If anaphylaxis or other significant hypersensitivity reaction occurs, administer appropriate medications (e.g., epinephrine) and provide supportive care as required. If a mild hypersensitivity reaction occurs, clinical judgment should be used regarding cautious readministration of Synagis.

Coagulation Disorders

Synagis is for intramuscular use only. As with any intramuscular injection, Synagis should be given with caution to children with thrombocytopenia or any coagulation disorder.

RSV Diagnostic Test Interference

Palivizumab may interfere with immunological-based RSV diagnostic tests such as some antigen detection-based assays. In addition, palivizumab inhibits virus replication in cell culture, and therefore may also interfere with viral culture assays. Palivizumab does not interfere with reverse transcriptase-polymerase chain reaction based assays. Assay interference could lead to false-negative RSV diagnostic test results. Therefore, diagnostic test results, when obtained, should be used in conjunction with clinical findings to guide medical decisions *[see Microbiology (12.4) in full Prescribing Information].*

Treatment of RSV Disease

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

Proper Administration

The single-dose vial of Synagis does not contain a preservative. Administration of Synagis should occur immediately after dose withdrawal from the vial. The vial should not be re-entered. Discard any unused portion.

ADVERSE REACTIONS

The most serious adverse reactions occurring with Synagis are anaphylaxis and other acute hypersensitivity reactions *[see Warnings and Precautions (5.1) in full Prescribing Information].*

Clinical Studies Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data described below reflect exposure to Synagis (n=1639) compared with placebo (n=1143) in children 3 days to 24.1 months of age at high risk of RSV-related hospitalization in two clinical trials. Trial 1 was conducted during a single RSV season and studied a total of 1502 children less than or equal to 24 months of age with BPD or infants with premature birth (less than or equal to 35 weeks gestation) who were less than or equal to 6 months of age at study entry. Trial 2 was conducted over four consecutive seasons among a total of 1287 children less than or equal to 24 months of age with hemodynamically significant congenital heart disease.

In Trials 1 and 2 combined, fever and rash were each reported more frequently among Synagis than placebo recipients, 27% versus 25%, and 12% versus 10%, respectively. Adverse reactions observed in the 153-patient crossover study comparing the liquid and lyophilized formulations were comparable for the two formulations, and were similar to those observed with Synagis in Trials 1 and 2.

Immunogenicity

In Trial 1, the incidence of anti-palivizumab antibody following the fourth injection was 1.1% in the placebo group and 0.7% in the Synagis group. In children receiving Synagis for a second season, one of the fifty-six children had transient, low titer reactivity. This reactivity was not associated with adverse events or alteration in serum concentrations. Immunogenicity was not assessed in Trial 2.

A trial of high-risk preterm children less than or equal to 24 months of age was conducted to evaluate the immunogenicity of the lyophilized formulation of Synagis (used in Trials 1 and 2 above) and the liquid formulation of Synagis. Three hundred seventy-nine children contributed to the 4 to 6 months post-final dose analysis. The rate of anti-palivizumab antibodies at this time point was low in both formulation groups (anti-palivizumab antibodies were not detected in any subject in the liquid formulation group and were detected in one subject in the lyophilized group (0.5%), with an overall rate of 0.3% for both treatment groups combined).

These data reflect the percentage of children whose test results were considered positive for antibodies to palivizumab in an enzyme-linked immunosorbent assay (ELISA) and are highly dependent on the sensitivity and specificity of the assay.

The ELISA has substantial limitations in detecting anti-palivizumab antibodies in the presence of palivizumab. Immunogenicity samples tested with the ELISA assay likely contained palivizumab at levels that may interfere with the detection of anti-palivizumab antibodies.

An electrochemical luminescence (ECL) based immunogenicity assay, with a higher tolerance for palivizumab presence compared to the ELISA, was used to evaluate the presence of anti-palivizumab antibodies in subject samples from two additional clinical trials. The rates of anti-palivizumab antibody positive results in these trials were 1.1% and 1.5%.

Postmarketing Experience

The following adverse 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.

Blood and Lymphatic System Disorders: severe thrombocytopenia (platelet count less than 50,000 per microliter)

General Disorders and Administration Site Conditions: injection site reactions

Limited information from post-marketing reports suggests that, within a single RSV season, adverse events after a sixth or greater dose of Synagis are similar in character and frequency to those after the initial five doses.

DRUG INTERACTIONS

No formal drug-drug interaction studies were conducted. In Trial 1, the proportions of children in the placebo and Synagis groups who received routine childhood vaccines, influenza vaccine, bronchodilators, or corticosteroids were similar and no incremental increase in adverse reactions was observed among children receiving these agents.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

Synagis is not indicated for use in females of reproductive potential.

Lactation

Risk Summary

Synagis is not indicated for use in females of reproductive potential.

Pediatric Use

The safety and effectiveness of Synagis in children older than 24 months of age at the start of dosing have not been established *[see Clinical Studies (14) in full Prescribing Information].*

OVERDOSAGE

Overdoses with doses up to 85 mg per kg have been reported in clinical studies and post-marketing experience with Synagis, and in some cases, adverse reactions were reported. In case of overdosage, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment instituted.

PATIENT COUNSELING INFORMATION

Advise the patient's caregiver to read the FDA-approved patient labeling (Patient Information)

Hypersensitivity Reactions

Inform the patient's caregiver of the signs and symptoms of potential hypersensitivity reactions, and advise the caregiver to seek medical attention immediately if the child experiences a severe hypersensitivity reaction to Synagis *[see Contraindications (4) and Warnings and Precautions (5.1) in full Prescribing Information].*

Administration

Advise the patient's caregiver that Synagis should be administered by a healthcare provider once a month during the RSV season by intramuscular injection and the importance of compliance with the full course of therapy *[see Dosage and Administration (2) in full Prescribing Information].*

Synagis® is a registered trademark of Arexis AB c/o Swedish Orphan Biovitrum AB (publ).

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Swedish Orphan Biovitrum AB (publ), Stockholm, Sweden

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