MedImmune

September 16, 2010

Office of Consumer Information and Insurance Oversight
Department of Health and Human Services
Room 445-G
Hubert H. Humphrey Building
200 Independence Ave., SW
Washington, DC 20201

RE: OCIIO-9992-IFC; Interim Final Rules for Group Health Plans and Health Insurance Issuers Relating to Coverage of Preventive Services Under the Patient Protection and Affordable Care Act; July 14, 2010

To Whom It May Concern:

I am writing on behalf of MedImmune to provide public comment about *Interim Final Rules for Group Health Plans and Health Insurance Issuers Relating to Coverage of Preventive Services Under the Patient Protection and Affordable Care Act* (OCIIO-9992-IFC) issued on July 14, 2010, which requires new plans and insurers to cover preventive care services for infants, children and adolescents without cost-sharing for the enrollee when such care is delivered by in-network providers. Under the Patient Protection and Affordable Care Act (PPACA), "no out-of-pocket costs shall apply with respect to infants, children and adolescents for evidence-informed preventive care and screenings provided for in comprehensive guidelines supported by the Health Resources and Services Administration (HRSA)."

MedImmune respectfully requests the agency's consideration in recognizing immunoprophylaxis for Respiratory Syncytial Virus (RSV) as an evidence-informed preventive care intervention included under the Interim Final Rules to ensure appropriate pediatric patients are not subject to cost-sharing measures for this prophylactic therapy.

According to the Healthcare.gov website[1], HRSA utilizes two sources of comprehensive guidelines for preventive care of infants, children and adolescents: the *Periodicity Schedule of the Bright Future Recommendations for Pediatric Preventive Health Care* and *the Uniform Panel of the Secretary's Advisory Committee for Heritable Disorders in Newborns and Children*.

Unfortunately, these guidelines are not necessarily inclusive of preventive services often needed for infants born prematurely, which accounts for 12.3 % of births in the U.S. in 2008.[2] For example, the *Bright Futures* guidelines consist of basic, routine outpatient preventive care to raise healthy children from infancy through adolescence. While there are broad, generalized references to premature infants, *Bright Futures* does not encompass the specific needs that are unique to premature infants. In fact, the *Bright Futures Periodicity Table* states, "The recommendations in this statement do not indicate an exclusive course of treatment or standard

of medical care. Variations, taking into account individual circumstances, may be appropriate."[3] Similarly, the *Secretary's Advisory Committee for Heritable Disorders in Newborns and Children* focuses on hereditary conditions and does not include preventive services for the premature infant.

MedImmune requests that HRSA recognize other evidence-informed preventive services for premature infants for inclusion in the interim final rule. Specifically, MedImmune requests consideration of Immunoprophylaxis for Respiratory Syncytial Virus (RSV). Both the American Academy of Pediatrics and the National Perinatal Association recognize RSV Immunoprophylaxis as an important preventive therapy for eligible premature infants.[4,5]

RSV is a common, seasonal virus that infects almost all children by the age of two.[6,7] RSV disease can be serious for premature infants, often leading to severe lung infections like pneumonia and bronchiolitis.[8,9] RSV disease is the leading cause of hospitalization in infants less than one year of age in the US.[8]

RSV-related morbidity and hospitalizations may be prevented through use of medication in appropriate patients. Synagis (palivizumab) is a monoclonal antibody manufactured by MedImmune that is the only FDA-approved medication for prophylaxis of RSV. According to U.S. Food & Drug Administration (FDA) approved labeling:

Synagis is a prescription medication that is used to help prevent a serious lung disease caused by respiratory syncytial virus (RSV) in infants and children at high risk for severe lung disease from RSV. Over one million children have been given Synagis. It is given as a shot, usually in the thigh muscle, each month during the RSV season. Children who develop an RSV infection while receiving Synagis should continue the monthly dosing schedule throughout the season.

Who should not receive Synagis?

Synagis should not be used in children who have ever had a severe allergic reaction to Synagis or its ingredients. Signs and symptoms of a severe allergic reaction could include: a drop in blood pressure; itchy rash; difficulty breathing; difficulty swallowing; swelling of the face; 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, be sure to tell your child's healthcare provider or get medical help right away.

What are the side effects with Synagis?

Possible, serious side effects include severe allergic reaction which may occur after any dose of Synagis. Unusual bruising and/or groups of tiny red spots on the skin have also been reported.

Common side effects of Synagis include fever, cold-like symptoms (upper respiratory tract infection), including runny nose and ear infection, and rash. Other possible side effects include skin reactions around the area where the shot was given (like redness, swelling, warmth or discomfort). In children born with certain heart problems, other possible side effects include bluish color of the skin and abnormal heart rhythms.

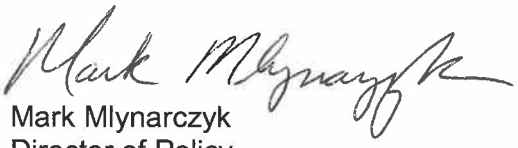
These are not all the possible side effects of Synagis. Tell your child's healthcare provider about any side effect that bothers your child or that does not go away.

Please see accompanying full product information, including information for patients and their caregivers

Because prevention against severe RSV disease is common practice for appropriate premature infants, MedImmune requests that HRSA consider recognition of RSV immunoprophylaxis as an evidence-informed preventive care intervention included under the HHS interim final regulations issued on July 14, 2010.

Thank you for your consideration.

Sincerely,



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1 At http://www.healthcare.gov/center/regulations/prevention/recommendations.html. Accessed on August 16, 2010.

2 At http://www.marchofdimes.com/peristats/whatsnew.aspx?id=39&dv=wn. Accessed August 16, 2010.

3 At http://brightfutures.aap.org/pdfs/AAP%20Bright%20Futures%20Periodicity%20Sched%20101107.pdf. Accessed on August 16, 2010.

4 AAP (American Academy of Pediatrics) Committee on Infectious Disease. Policy Statement—Modified Recommendations for the use of palivizumab for the prevention of respiratory syncytial virus infections. Pediatrics. 2009;124:1216-1226.

5 At http://www.nationalperinatal.org/advocacy/pdf/Respiratory-Syncytial-Virus-Prevention-2010.pdf. Accessed on August 30, 2010.

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8113

SYNAGIS® (PALIVIZUMAB)

for Intramuscular Administration **Rx only**

DESCRIPTION: Synagis (palivizumab) is a humanized monoclonal antibody (IgG1κ) produced by recombinant DNA technology, directed to an epitope in the A antigenic site of the F protein of respiratory syncytial virus (RSV). Synagis is a composite of human (95%) and murine (5%) antibody sequences. The human heavy chain sequence was derived from the constant domains of human IgG1 and the variable framework regions of the V_H genes Cor (1) and Cess (2). The human light chain sequence was derived from the constant domain of Cκ and the variable framework regions of the V_L gene K104 with Jκ -4 (3). The murine sequences were derived from a murine monoclonal antibody, Mab 1129 (4), in a process that involved the grafting of the murine complementarity determining regions into the human antibody frameworks. Synagis is composed of two heavy chains and two light chains and has a molecular weight of approximately 148,000 Daltons.

Synagis is supplied as a sterile, preservative-free liquid solution at 100 mg/mL to be administered by intramuscular injection (IM). Thimerosal or other mercury containing salts are not used in the production of Synagis. The solution has a pH of 6.0 and should appear clear or slightly opalescent.

Each 100 mg single-dose vial of Synagis liquid solution contains 100 mg of Synagis, 3.9 mg of histidine, 0.1 mg of glycine, and 0.5 mg of chloride in a volume of 1 mL.

Each 50 mg single-dose vial of Synagis liquid solution contains 50 mg of Synagis, 1.9 mg of histidine, 0.06 mg of glycine, and 0.2 mg of chloride in a volume of 0.5 mL.

CLINICAL PHARMACOLOGY: *Mechanism of Action:* Synagis exhibits neutralizing and fusion-inhibitory activity against RSV. These activities inhibit RSV replication in laboratory experiments. Although resistant RSV strains may be isolated in laboratory studies, a panel of 57 clinical RSV isolates were all neutralized by Synagis (5). Synagis serum concentrations of ≥ 40 mcg/mL have been shown to reduce pulmonary RSV replication in the cotton rat model of RSV infection by 100-fold (5). The *in vivo* neutralizing activity of the active ingredient in Synagis was assessed in a randomized, placebo-controlled study of 35 pediatric patients tracheally intubated because of RSV disease. In these patients, Synagis significantly reduced the quantity of RSV in the lower respiratory tract compared to control patients (6).

Pharmacokinetics: In pediatric patients < 24 months of age without congenital heart disease (CHD), the mean half-life of Synagis was 20 days and monthly intramuscular doses of 15 mg/kg achieved mean ± SD 30 day trough serum drug concentrations of 37 ± 21 mcg/mL after the first injection, 57 ± 41 mcg/mL after the second injection, 68 ± 51 mcg/mL after the third injection and 72 ± 50 mcg/mL after the fourth injection (7). Trough concentrations following the first and fourth Synagis dose were similar in children with CHD and in non-cardiac patients. In pediatric patients given Synagis for a second season, the mean ± SD serum concentrations following the first and fourth injections were 61 ± 17 mcg/mL and 86 ± 31 mcg/mL, respectively.

In 139 pediatric patients ≤ 24 months of age with hemodynamically significant CHD who received Synagis and underwent cardio-pulmonary bypass for open-heart surgery, the mean ± SD serum Synagis concentration was 98 ± 52 mcg/mL before bypass and declined to 41 ± 33 mcg/mL after bypass, a reduction of 58% (see *DOSAGE AND ADMINISTRATION*). The clinical significance of this reduction is unknown.

Specific studies were not conducted to evaluate the effects of demographic parameters on Synagis systemic exposure. However, no effects of gender, age, body weight or race on Synagis serum trough concentrations were observed in a clinical study with 639 pediatric patients with CHD (≤ 24 months of age) receiving five monthly intramuscular injections of 15 mg/kg of Synagis.

The pharmacokinetics and safety of Synagis liquid solution and Synagis lyophilized formulation administered IM at 15 mg/kg were studied in a cross-over trial of 153 pediatric patients ≤ 6 months of age with a history of prematurity. The results of this trial indicated that the trough serum concentrations of palivizumab were comparable between the liquid solution and the lyophilized formulation, which was the formulation used in the clinical studies described below.

CLINICAL STUDIES: The safety and efficacy of Synagis were assessed in two randomized, double-blind, placebo-controlled trials of prophylaxis against RSV infection in pediatric patients at high risk of an RSV-related hospitalization. Trial 1 was conducted during a single RSV season and studied a total of 1,502 patients ≤ 24 months of age with bronchopulmonary dysplasia (BPD) or infants with premature birth (≤ 35 weeks gestation) who were ≤ 6 months of age at study entry (7). Trial 2 was conducted over four consecutive seasons among a total of 1287 patients ≤ 24 months of age with hemodynamically significant congenital heart disease. In both trials participants received 15 mg/kg Synagis or an equivalent volume of placebo IM monthly for five injections and were followed for 150 days from randomization. In Trial 1, 99% of all subjects completed the study and 93% completed all five injections. In Trial 2, 96% of all subjects completed the study and 92% completed all five injections. The incidence of RSV hospitalization is shown in Table 1.

Table 1: Incidence of RSV Hospitalization by Treatment Group

Trial		Placebo	Synagis	Difference Between Groups	Relative Reduction	p-Value
Trial 1 Impact-RSV	N	500	1002			
	Hospitalization	53 (10.6%)	48 (4.8%)	5.8%	55%	< 0.001
Trial 2 CHD	N	648	639			
	Hospitalization	63 (9.7%)	34 (5.3%)	4.4%	45%	0.003

In Trial 1, the reduction of RSV hospitalization was observed both in patients with BPD (34/266 [12.8%] placebo vs. 39/496 [7.9%] Synagis), and in premature infants without BPD (19/234 [8.1%] placebo vs. 9/506 [1.8%] Synagis). In Trial 2, reductions were observed in acyanotic (36/305 [11.8%] placebo versus 15/300 [5.0%] Synagis) and cyanotic children (27/343 [7.9%] placebo versus 19/339 [5.6%] Synagis).

The clinical studies do not suggest that RSV infection was less severe among RSV hospitalized patients who received Synagis compared to those who received placebo.

INDICATIONS AND USAGE: Synagis is indicated for the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) in pediatric patients at high risk of RSV disease. Safety and efficacy were established in infants with bronchopulmonary dysplasia (BPD), infants with a history of premature birth (≤ 35 weeks gestational age), and children with hemodynamically significant congenital heart disease (CHD) (see *CLINICAL STUDIES*).

CONTRAINDICATIONS: Synagis should not be used in pediatric patients with a history of a severe prior reaction to Synagis or other components of this product.

WARNINGS: Very rare cases of anaphylaxis including anaphylactic shock (< 1 case per 100,000 patients) have been reported following initial exposure or re-exposure to Synagis (see *ADVERSE REACTIONS, Post-Marketing Experience*). Severe acute hypersensitivity reactions, estimated to be rare, (< 1 case per 1,000 patients) have also been reported on initial exposure or re-exposure to Synagis (see *ADVERSE REACTIONS, Post-Marketing Experience*). If a severe hypersensitivity reaction occurs, therapy with Synagis should be permanently discontinued. If milder hypersensitivity reactions occur, caution should be used on readministration of Synagis. **If anaphylaxis or severe allergic reactions occur, administer appropriate medications (e.g., epinephrine) and provide supportive care as required.**

PRECAUTIONS: *General:* Synagis is for intramuscular use only. As with any intramuscular injection, Synagis should be given with caution to patients with thrombocytopenia or any coagulation disorder.

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

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.

Drug Interactions: No formal drug-drug interaction studies were conducted. In Trial 1, the proportions of patients 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 patients receiving these agents.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Carcinogenesis, mutagenesis and reproductive toxicity studies have not been performed.

Pregnancy: Pregnancy Category C: Synagis is not indicated for adult usage and animal reproduction studies have not been conducted. It is also not known whether Synagis can cause fetal harm when administered to a pregnant woman or could affect reproductive capacity.

ADVERSE REACTIONS: The most serious adverse reactions occurring with Synagis treatment are anaphylaxis and other acute hypersensitivity reactions (see *WARNINGS*). The adverse reactions most commonly observed in Synagis-treated patients were upper respiratory tract infection, otitis media, fever, rhinitis, rash, diarrhea, cough, vomiting, gastroenteritis, and wheezing. Upper respiratory tract infection, otitis media, fever, and rhinitis occurred at a rate of 1% or greater in the Synagis group compared to placebo (Table 2).

Because clinical trials are conducted under widely varying conditions, adverse event 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 adverse reaction information does, however, provide a basis for identifying the adverse events that appear to be related to drug use and a basis for approximating rates.

The data described reflect Synagis exposure for 1641 pediatric patients of age 3 days to 24.1 months in Trials 1 and 2. Among these patients, 496 had bronchopulmonary dysplasia, 506 were premature birth infants less than 6 months of age, and 639 had congenital heart disease. Adverse events observed in the 153 patient crossover study comparing the liquid and lyophilized formulations were similar between the two formulations, and similar to the adverse events observed with Synagis in Trials 1 and 2.

Table 2: Adverse Events Occurring at a Rate of 1% or Greater More Frequently in Patients† Receiving Synagis

Event	Synagis (n=1641) n (%)	Placebo (n=1148) n (%)
Upper respiratory infection	830 (50.6)	544 (47.4)
Otitis media	597 (36.4)	397 (34.6)
Fever	446 (27.1)	289 (25.2)
Rhinitis	439 (26.8)	282 (24.6)
Hernia	68 (4.1)	30 (2.6)
SGOT Increase	49 (3.0)	20 (1.7)

†Cyanosis (Synagis [9.1%]/placebo [6.9%]) and arrhythmia (Synagis [3.1%]/placebo [1.7%]) were reported during Trial 2 in CHD patients.

Immunogenicity

In Trial 1, the incidence of anti-Synagis antibody following the fourth injection was 1.1% in the placebo group and 0.7% in the Synagis group. In pediatric patients receiving Synagis for a second season, one of the fifty-six patients 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.

These data reflect the percentage of patients whose test results were considered positive for antibodies to Synagis in an ELISA assay, and are highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody positivity in an assay may be influenced by several factors including sample handling, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to Synagis with the incidence of antibodies to other products may be misleading.

With any monoclonal antibody, the possibility exists that a liquid solution may be more immunogenic than a lyophilized formulation. The relative immunogenicity rates between the lyophilized formulation, used in Trials 1 and 2 above, and the liquid solution have not yet been established.

Post-Marketing Experience

The following adverse reactions have been identified and reported during post-approval use of Synagis. Because the reports of these reactions are voluntary and the population is of uncertain size, it is not always possible to reliably estimate the frequency of the reaction or establish a causal relationship to drug exposure.

Blood and Lymphatic System Disorders: severe thrombocytopenia (platelet count < 50,000/microliter)

General Disorders and Administration Site Conditions: injection site reactions

Immune System Disorders: severe acute hypersensitivity reactions and anaphylaxis (including dyspnea, cyanosis, respiratory failure, urticaria, pruritus, angioedema, hypotonia, hypotension, and unresponsiveness) have been reported (see *WARNINGS*). None of the reported hypersensitivity reactions were fatal. The relationship between these reactions and the development of antibodies to Synagis is unknown.

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.

OVERDOSAGE: No data from clinical studies are available on overdosage. No toxicity was observed in rabbits administered a single intramuscular or subcutaneous injection of Synagis at a dose of 50 mg/kg.

DOSAGE AND ADMINISTRATION: The recommended dose of Synagis is 15 mg/kg of body weight. Patients, including those who develop an RSV infection, should continue to receive monthly doses throughout the RSV season. The first dose should be administered prior to commencement of 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*). Patients undergoing cardio-pulmonary bypass should receive a 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.

Synagis should be administered in a dose of 15 mg/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 per month = patient weight (kg) x 15 mg/kg ÷ 100 mg/mL of Synagis. Injection volumes over 1 mL should be given as a divided dose.

Administration of Synagis

- **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 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.
- To prevent the transmission of hepatitis viruses or other infectious agents from one person to another, sterile disposable syringes and needles should be used. DO NOT reuse syringes and needles.

HOW SUPPLIED: Synagis is supplied in single-dose vials as a preservative-free, sterile liquid solution at 100 mg/mL for IM injection.

50 mg vial NDC 60574-4114-1
The 50 mg vial contains 50 mg Synagis in 0.5 mL.

100 mg vial NDC 60574-4113-1
The 100 mg vial contains 100 mg Synagis in 1 mL.

There is no latex in the rubber stopper used for sealing vials of Synagis. Upon receipt and until use, Synagis should be stored between 2°C and 8°C (35.6°F and 46.4°F) in its original container. DO NOT freeze. DO NOT use beyond the expiration date.

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MedImmune

Manufactured by:
MedImmune, LLC
Gaithersburg, MD 20878
U.S. Gov't. License No. 1799
(1-877-633-4411)

Revision Date: July 2010 RAL-SYNV13
Component No.: 7739

Information for Patients and Their Caregivers

SYNAGIS® (SĬ-nă-jĭs)

(palivizumab)

Read this Patient Information before your child starts receiving SYNAGIS and before each injection. The information may have changed. This leaflet does not take the place of talking with your child's healthcare provider about your child's condition or treatment.

What is SYNAGIS?

SYNAGIS is a prescription medication that is used to help prevent a serious lung disease caused by Respiratory Syncytial Virus (RSV). Your child is prescribed SYNAGIS because he or she is at high risk for severe lung disease from RSV.

SYNAGIS contains man-made, disease-fighting proteins called antibodies. These antibodies help prevent RSV disease. Children at high risk for severe RSV disease often do not have enough of their own antibodies. SYNAGIS is used in certain groups of children to help prevent severe RSV disease by increasing protective RSV antibodies.

SYNAGIS is not used to treat the symptoms of RSV disease, once a child already has it. It is only used to prevent RSV disease.

SYNAGIS is not for adults.

Who should not receive SYNAGIS?

Your child should not receive SYNAGIS if they have ever had a severe allergic reaction to it or any of its ingredients. Signs and symptoms of a severe allergic reaction could include:

- a drop in blood pressure
- severe rash, hives or itching skin
- difficult, rapid or irregular breathing
- closing of the throat, difficulty swallowing
- swelling of the lips, tongue, or face
- bluish color of skin, lips or under fingernails
- muscle weakness or floppiness
- unresponsiveness

See the end of this leaflet for a list of ingredients in SYNAGIS.

What should I tell my child's healthcare provider before my child receives SYNAGIS?

Tell your child's healthcare provider about:

- **Any reactions** you believe your child has ever had to SYNAGIS.
- All your child's medical problems, including **any bleeding or bruising problems.** SYNAGIS is given by injection. If your child has a problem with bleeding or bruises easily, an injection could cause a problem.
- **All the medicines your child takes, including prescription and non-prescription medicines, vitamins, and herbal supplements.** Especially tell your child's healthcare provider if your child takes a blood thinner medicine.

How is SYNAGIS given?

- SYNAGIS is given as a monthly injection, usually in the thigh (leg) muscle, by your child's healthcare provider. Your child's healthcare provider will prescribe the amount of SYNAGIS that is right for your child (based on their weight).
- Your child's healthcare provider will give you detailed instructions on when SYNAGIS will be given.
    - "RSV season" is a term used to describe the time of year when RSV infections most commonly occur (usually fall through spring). During this time, when RSV is most active, your child will need to receive SYNAGIS shots. Your child's healthcare provider can tell you when the RSV season starts in your area.
    - Your child should receive their **first SYNAGIS shot before the RSV season starts** to help protect them before RSV becomes active. If the season has already started, your child should receive their first SYNAGIS shot as soon as possible to help protect them when exposure to the virus is more likely.
    - **SYNAGIS is needed every 28-30 days during the RSV season.** Each dose of SYNAGIS helps protect your child from severe RSV disease for about a month. **Keep all appointments with your child's healthcare provider.**
- **If your child misses an injection, talk to your healthcare provider and schedule another injection as soon as possible.**
- Your child may still get severe RSV disease after receiving SYNAGIS. Talk to your child's healthcare provider about what symptoms to look for.
- If your child already has an RSV infection and is sick, they still need to get their scheduled SYNAGIS injections to help prevent severe disease from new RSV infections.
- If your child has certain types of heart disease and has corrective surgery, your healthcare provider may need to give your child an additional SYNAGIS injection soon after surgery.

What are the possible side effects of SYNAGIS?

Over one million babies have been given SYNAGIS. Like all medicines, SYNAGIS has been associated with side effects in some patients. Most of the time, the side effects are not serious. If side effects do occur, your child may need medical attention.

Possible, serious side effects include:

- Severe allergic reactions (may occur after any dose of SYNAGIS). See "Who should not take SYNAGIS?" for a list of signs and symptoms.
- Unusual bruising and/or groups of tiny red spots on the skin.

Call your child's healthcare provider or get medical help right away if your child has any of the serious side effects listed above after any dose of SYNAGIS.

Common side effects of SYNAGIS include:

- fever
- cold-like symptoms (upper respiratory infection), including runny nose and ear infection
- rash

Other possible side effects include skin reactions around the area where the shot was given (like redness, swelling, warmth, or discomfort).

In children born with certain types of heart disease, other possible side effects include bluish color of the skin, lips or under fingernails and abnormal heart rhythms.

These are not all the possible side effects of SYNAGIS. Tell your child's healthcare provider about any side effect that bothers your child or that does not go away.

Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or call MedImmune at 1-877-633-4411.

General Information about SYNAGIS

Medicines are sometimes prescribed for purposes other than those listed in Patient Information leaflets.

This leaflet summarizes important information about SYNAGIS. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about SYNAGIS that is written for health professionals.

For more information, go to www.synagis.com or call 1-877-633-4411.

What are the ingredients in SYNAGIS?

Active Ingredient: palivizumab

Inactive Ingredients: histidine, glycine, and chloride

What is RSV?

Respiratory Syncytial Virus (RSV) is a common virus that is easily spread from person to person. RSV infects nearly all children by their second birthday. In most children, RSV infection is usually no worse than a bad cold. For some children, RSV infection can cause serious lung disease (like pneumonia and bronchiolitis) or breathing problems, and affected children may need to be admitted to the hospital or need emergency care.

Children who are more likely to get severe RSV disease (high risk children) include babies born prematurely (35 weeks or less), or babies born with certain heart or lung problems.

MedImmune

Manufactured by: MedImmune, LLC
Gaithersburg, MD 20878

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