Palivizumab (Synagis®) Solution for Intramuscular Injection

Description[1,2]:

Humanized murine immunoglobulin monoclonal antibody, manufactured by MedImmune, the global biologics research and development arm of AstraZeneca

Indication[1]:

Prevention of serious disease of the lower respiratory tract attributable to respiratory syncytial virus[2] in pediatric patients at high risk of contracting this virus

Population[1,2]:

Safety and efficacy have been established in:

- **Children with bronchopulmonary dysplasia (BPD)**
- **Infants with a history of premature birth (gestational age ≤35 weeks)**
- **Children with hemodynamically significant congenital heart disease (CHD)**

Mechanism of action[1]:

Binds the fusion protein of RSV in the lower respiratory tract, preventing the structural changes necessary for the viral envelope fusion to the host; provides passive immunity.

How supplied	Preservative-free, single-dose liquid solution vials • 0.5 mL vial: 50 mg • 1 mL vial: 100 mg
Storage	Between 2 and 8°C in its original container Vials should not be shaken or diluted

References: 1. Synagis® [package insert]. Gaithersburg, MD: MedImmune, LLC; 2014. 2. MedImmune. About MedImmune. *MedImmune* 2013; https://www.medimmune.com/about-medimmune. Accessed August 24, 2014. 3. IMpact-RSV-Study-Group. *Pediatrics.* 1998;102(3):531-537. Last reviewed Nov. 2014.

Dosage and administration[1]:

The manufacturer recommends 15 mg/kg monthly intramuscular (IM) injections x maximum of 5 doses prior to and throughout the RSV season (typically November through April).

- Patients only require enough doses to carry them through the season[3]. Therefore, children born during the RSV season will require fewer than 5 doses.
- The smallest vial size possible should be used
- Administration should occur immediately after vial opening.

$$\text{Dose volume} = \frac{(Patient\ weight\ (in\ kg*)\ \times 15\ mg/kg)}{100\ mg/ml}$$

*1 kg=2.205 lbs

Dosing Table

Volume (mL)	Number of vials	Maximum dosage	Maximum body weight
0.5	1	50 mg	3.3 kg (7.3 lb)
1	1	100 mg	6.7 kg (14.7 lb)
1.5	2 (0.5 mL + 1 mL)	150 mg	10 kg (22 lb)
2	2 (1 mL + 1 mL)	200 mg	13.3 kg (29.3 lb)

Safety Information[1]

Adverse Events

- Anaphylaxis
- Acute hypersensitivity
- Clinical trial results:
  - ≥1%: fever, diarrhea, nervousness
  - ≤1%: rash, AST/ALT elevation, liver abnormalities, URI, vomit, cough, rhinitis
- Post marketing surveillance: thrombocytopenia, injection site reactions

Caution

- IM injection: coagulation disorders, thrombocytopenia
- False negatives possible: antigen detection-based assays or viral culture assays

Contraindication

- Previous episode of anaphylaxis due to palivizumab or components

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Approval Data:

Palivizumab was approved by the Food and Drug Administration (FDA) in 1998.[1] The pivotal trial leading to approval of palivizumab was a Phase III study conducted by the IMpact-RSV group.[3]

Trial Design and Population

- Multicenter, randomized, double-blind, placebo-controlled trial conducted in the United States, Canada, and United Kingdom during the 1996-1997 RSV season
- Purpose: to evaluate the safety and efficacy of palivizumab for RSV prophylaxis in high-risk infants
- High-risk: gestational age ≤35 weeks or diagnosis of BPD
- Primary endpoint: hospitalization due to RSV infection

Intervention and Monitoring

- Treatment group: palivizumab 15 mg/kg IM every 30 days x 5 doses
- Placebo group:equal volume of placebo liquid IM every 30 days x 5 doses
- Subjects were monitored for up to 150 days, or 1 month following their last injection
- Hospitalized subjects were monitored throughout their hospitalization with a focus on disease severity, need for supplemental oxygen and other pulmonary support measures

Results

- 1502 children were randomized, 500 to the placebo group and 1002 to the treatment group
- 99% completed the study through the protocol follow-up period; 94% of the placebo group and 92% of the palivizumab group received all 5 injections
- Compared with the placebo group, palivizumab recipients showed a 55% reduction in the rate of RSV-related hospitalization (10.6% placebo vs. 4.8% palivizumab, p=0.00004)
- Premature infants without BPD who received palivizumab showed a 78% reduction with palivizumab vs. placebo (8.1% placebo vs. 1.8% palivizumab, p<0.001); those with BPD showed a 39% reduction (12.8% placebo vs. 7.9% palivizumab, p=0.038)

Conclusion:

Palivizumab was found to be effective in the prevention of RSV in high-risk infants and generally well-tolerated.

References: 1. Synagis® [package insert]. Gaithersburg, MD: MedImmune, LLC; 2014. 2. MedImmune. About MedImmune. *MedImmune* 2013; https://www.medimmune.com/about-medimmune. Accessed August 24, 2014. 3. IMpact-RSV-Study-Group. *Pediatrics.* 1998;102(3):531-537. Last reviewed Nov. 2014.