

Package Insert

Immune Serum Globulin (Human)

DESCRIPTION:

Immune Serum Globulin (Human) [ISG] is a sterile solution of immunoglobulin, primarily immunoglobulin G (IgG), containing $16.5 \pm 1.5\%$ protein. It is prepared by cold alcohol fractionation of pooled plasma. All plasma units have been tested and found non-reactive for hepatitis B surface antigen (HBsAg). ISG contains the mercurial preservative, sodium ethylmercurithiosalicylate (thimerosal), at a concentration of 100 mg per liter and * M glycine. The pH of the solution has been adjusted to 6.8 ± 0.4 with *.

CLINICAL PHARMACOLOGY/BIOLOGICAL ACTIVITY:

Peak blood levels of immunoglobulin G are obtained approximately 2 days after intramuscular injection of ISG (1). The half-life of IgG in the circulation of individuals with normal IgG levels is 23 days (2).

Passive immunization with ISG modifies hepatitis A, prevents or modifies measles, and provides replacement therapy in persons with hypo- or agammaglobulinemia. ISG is not standardized with respect to antibody titers against hepatitis B surface antigen (HBsAg) and should be used for prophylaxis of viral hepatitis type B (HBV) only when Hepatitis B Immune Globulin is not available (3).

* The manufacturer should fill in and modify so that this paragraph is an accurate description of the product.

ISG may be of benefit in women who have been exposed to rubella in the first trimester of pregnancy and who would not consider a therapeutic abortion (4). ISG may also be used in immunosuppressed patients for passive immunization against varicella if Zoster Immune Globulin is not available (4).

ISG is not indicated for routine prophylaxis or treatment of rubella, poliomyelitis, or mumps. It is not indicated for allergy or asthma in patients who have normal levels of immunoglobulin (4).

INDICATIONS AND DOSE:

Hepatitis A

The prophylactic value of ISG is greatest when given before or soon after exposure to hepatitis A. ISG is not indicated in persons with clinical manifestations of hepatitis A or in those exposed more than 2 weeks previously. ISG in a dose of 0.01 ml/lb (0.02 ml/kg) is recommended for household and institutional hepatitis A case contacts.

The following doses of ISG are recommended for persons who plan to travel in areas where hepatitis A is common (3):

<u>Length of Stay</u>	<u>Dose Volume</u>
Less than 3 months	0.02 ml/kg
3 months or longer	0.05 ml/kg (repeat every 4-6 months)

Hepatitis B

Hepatitis B Immune Globulin (Human) [HBIG] is indicated for post-exposure prophylaxis following accidental needle-sticks or oral ingestion of HBsAg positive material. If this is unavailable, then ISG at a dose of

0.06 ml/kg should be administered as soon after exposure as possible of (preferably within 7 days) and repeated 25-30 days later.

Measles (Rubeola)

ISG should be given in a dose of 0.1 ml/lb (0.2 ml/kg) to prevent or modify measles in a susceptible person exposed less than 6 days previously (5). (A susceptible person is one who has not been vaccinated and has not had measles previously). ISG may be especially indicated for susceptible household contacts of measles patients, particularly contacts under one year of age, for whom the risk of complications is highest (5). ISG and measles vaccine should not be given at the same time (5). If a child is older than 9 months and has receive ISG, he should be given measles vaccine about 3 months later, when the measles antibody titer will have disappeared.

If a susceptible child exposed to measles has leukemia, lymphoma or loss of cell-mediated immunity, or is undergoing chronic immunosuppression, 20 to 30 ml of ISG should be given immediately. Children who are immunosuppressed or have an immune deficiency disease should not receive measles vaccine or any other live viral vaccine.

Immunoglobulin Deficiency

In patients with immunoglobulin deficiencies, ISG may prevent serious infection if circulating IgG levels of ~200 mg/100 ml plasma are maintained. However, ISG may not prevent chronic infections of the external secretory tissues such as the respiratory and gastrointestinal tract. The recommended dosage is 0.66 ml/kg (at least 100 mg/kg) given every 3 to 4 weeks (4). A double

dose is given at onset of therapy: some patients may require more frequent injections.

Prophylactic therapy, especially against infections due to encapsulated bacteria, is effective in Bruton-type, sex-linked congenital agammaglobulinemia, agammaglobulinemia associated with thymoma and acquired agammaglobulinemia.

Varicella

Passive immunization against varicella in immunosuppressed patients is best accomplished by use of Zoster Immune Globulin (ZIG). If ZIG is unavailable, ISG at a dose of 0.6 to $\frac{1}{2}$ ml/kg, promptly given, may also modify varicella (4).

Rubella

The routine use of ISG for prophylaxis of rubella in early pregnancy is of dubious value and cannot be justified (4). Some studies suggest that the use of ISG in exposed, susceptible women can lessen the likelihood of infection and fetal damage; therefore 20 ml of ISG may benefit those women who will not consider a therapeutic abortion (4).

CONTRATINDICATIONS:

ISG should not be given to persons with isolated immunoglobulin A (IgA) deficiency. Such persons have the potential for developing antibodies to IgA and could have anaphylactic reactions to subsequent administration of blood products that contain IgA (6).

IG should not be administered to patients who have severe thrombocytopenia or any coagulation disorder that would contraindicate Intramuscular injections.

ISG should be given with caution to patients with a history of prior systemic allergic reactions following the administration of human immunoglobulin preparations (6)

PRECAUTIONS:

ISG should not be administered intravenously because of the potential for serious reactions. Injections should be made intramuscularly, and care should be taken to draw back on the plunger of the syringe before injection in order to be certain that the needle is not a blood vessel.

Although systemic reactions to intramuscularly administered immunoglobulin preparations are rare, epinephrine should be available for treatment of acute allergic symptoms.

CLINICAL AND LABORATORY TESTS:

None required.

CLINICALLY SIGNIFICANT PRODUCT INTERACTIONS:

Antibodies in the globulin preparation may interfere with the response to live viral vaccines such as measles, mumps, and rubella. Therefore, use of such vaccines should be deferred until approximately three months after ISG administration.

No interactions with other products are known.

PREGNANCY:

Pregnancy is not a contraindication to the administration of ISG.

ADVERSE REACTIONS:

Local pain and tenderness at the injection site, urticaria, and angioedema may occur. Anaphylactic reactions, although rare,

have been reported following the infection of human immune globulin preparations (6). Anaphylaxis is more likely to occur if ISG is given intravenously; therefore ISG must be administered only intramuscularly.

ADMINISTRATION:

ISG is administered intramuscularly (see PRECAUTIONS), preferably in the gluteal region. Doses over 10 ml should be divided and injected into several muscle sites to reduce local pain and discomfort.

Dosage is describe above under INDICATIONS AND DOSE.

CAUTION:

Federal (U.S.A.) law prohibits dispensing without prescription.

STORAGE:

Store at 2 to 8 °C. Do not freeze. Do not use after expiration date.

HOW SUPPLIED:

ISG is supplied in *, * and * ml vials.

References

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3. Morbidity and Mortality Weekly Report, December 30, 1977 (Vol. 26,
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4. Report of the Committee on Infectious Disease, American Academy of
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5. Morbidity and Mortality Weekly Report, November 19, 1976 (Vol. 25,
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6. Fudenberg, HH: Sensitization to immunoglobulins and hazards of
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