Immune Globulin (Human)

Gama**STAN**® S/D

Solvent/Detergent Treated

DESCRIPTION

Immune Globulin (Human) — Gama**STAN**® S/D treated with solvent/detergent is a colorless to pale yellow or pink sterile solution of immune globulin for intramuscular administration; it is preservative-free and latex-free. Gama**STAN** S/D is prepared by cold ethanol fractionation from human plasma. The immune globulin is isolated from solubilized Cohn fraction II. The fraction II solution is adjusted to a final concentration of 0.3% tri-n-butyl phosphate (TNBP) and 0.2% sodium cholate. After the addition of solvent (TNBP) and detergent (sodium cholate), the solution is heated to 30°C and maintained at that temperature for not less than 6 hours. After the viral inactivation step, the reactants are removed by precipitation, filtration and finally ultrafiltration and diafiltration. Gama**STAN** S/D is formulated as a 15–18% protein solution at a pH of 6.4–7.2 in 0.21–0.32 M glycine. Gama**STAN** S/D is then incubated in the final container for 21–28 days at 20–27°C.

The removal and inactivation of spiked model enveloped and non-enveloped viruses during the manufacturing process for Gama**STAN** S/D has been validated in laboratory studies. Human Immunodeficiency Virus, Type 1 (HIV-1), was chosen as the relevant virus for blood products; Bovine Viral Diarrhea Virus (BVDV) was chosen to model Hepatitis C virus; Pseudorabies virus (PRV) was chosen to model Human Herpes viruses and other large enveloped DNA viruses; and Reo virus type 3 (Reo) was chosen to model non-enveloped viruses and for its resistance to physical and chemical inactivation. Removal of model enveloped and non-enveloped viruses is achieved at two steps in the Cohn fractionation process leading to the collection of Cohn Fraction II: the precipitation and removal of Fraction III in the processing of Fraction II + IIIW suspension to Effluent III and the filtration step in the processing of Effluent III to Filtrate III. Inactivation of enveloped viruses is achieved at the time of treatment of solubilized Cohn Fraction II with TNBP/sodium cholate.

Additionally, the manufacturing process was investigated for its capacity to decrease the infectivity of an experimental agent of transmissible spongiform encephalopathy (TSE), considered as a model for the vCJD and CJD agents.(11-14)

Studies of the Gama**STAN** S/D manufacturing process demonstrate that TSE clearance is achieved during the Pooled Plasma to Effluent III Fractionation Process (6.7 $\log_{10}$). These studies provide reasonable assurance that low levels of CJD/vCJD agent infectivity, if present in the starting material, would be removed.

CLINICAL PHARMACOLOGY

Peak levels of immunoglobulin G are obtained approximately 2 days after intramuscular injection of Gama**STAN** S/D.(1) The half-life of IgG in the circulation of individuals with normal IgG levels is 23 days.(2)

Passive immunization with Gama**STAN** S/D modifies hepatitis A and prevents or modifies measles. Gama**STAN** S/D is not standardized with respect to antibody titers against hepatitis B surface antigen (HBsAg) and should not be used for prophylaxis of viral hepatitis type B. Prophylactic treatment to prevent hepatitis B can best be accomplished with use of Hepatitis B Immune Globulin (Human), often in combination with Hepatitis B Vaccine.(3)

Gama**STAN** S/D may be of benefit in women who have been exposed to rubella in the first trimester of pregnancy and who will not consider a therapeutic abortion.(4) Gama**STAN** S/D may also be considered for use in immunocompromised patients for passive immunization against varicella if Varicella-Zoster Immune Globulin (Human) is not available.(5)

Immune Globulin (Human) is not indicated for routine prophylaxis or treatment of rubella, poliomyelitis, mumps, or varicella. It is not indicated for allergy or asthma in patients who have normal levels of immunoglobulin.(6)

In a clinical study in eight healthy human adults receiving another hyperimmune immune globulin product treated with solvent/detergent, Rabies Immune Globulin (Human), Hyper**RAB**® S/D, prepared by the same manufacturing process, detectable passive antibody titers were observed in the serum of all subjects by 24 hours post injection and persisted through the 21 day study period. These results suggest that passive immunization with immune globulin products is not affected by the solvent/detergent treatment.

INDICATIONS AND USAGE

Hepatitis A

The prophylactic value of Gama**STAN** S/D is greatest when given before or soon after exposure to hepatitis A. Gama**STAN** S/D is not indicated in persons with clinical manifestations of hepatitis A or in those exposed more than 2 weeks previously.

Measles (Rubeola)

To prevent or modify measles give Gama**STAN** S/D in a susceptible person exposed fewer than 6 days previously.(7) A susceptible person is one who has not been vaccinated and has not had measles previously. Gama**STAN** S/D may be especially indicated for susceptible household contacts of measles patients, particularly contacts under 1 year of age, for whom the risk of complications is highest.(7) **GamaSTAN S/D and measles vaccine should not be given at the same time**.(7) If a child is older than 12 months and has received Gama**STAN** S/D, 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 is immunocompromised, Gama**STAN** S/D should be given immediately.(8)

Do not administer measles vaccine or any other live viral vaccine to children who are immunocompromised.

Varicella

Passive immunization against varicella in immunosuppressed patients is best accomplished by use of Varicella-Zoster Immune Globulin (Human) [VZIG]. If VZIG is unavailable, Gama**STAN** S/D, promptly given, may also modify varicella.(5)

Rubella

The routine use of Gama**STAN** S/D for prophylaxis of rubella in early pregnancy is of dubious value and cannot be justified.(6) Some studies suggest that the use of Gama**STAN** S/D in exposed, susceptible women can lessen the likelihood of infection and fetal damage; therefore, Gama**STAN** S/D may benefit those women who will not consider a therapeutic abortion.(4)

CONTRAINDICATIONS

Do not give Gama**STAN** S/D 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.(9)

Do not give Gama**STAN** S/D to patients who have severe thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injections.

WARNINGS

WARNING: THROMBOSIS

Thrombosis may occur with immune globulin products, including GamaSTAN S/D. Risk factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling central vascular catheters, hyperviscosity, and cardiovascular risk factors. Thrombosis may occur in the absence of known risk factors. (see PRECAUTIONS: Thrombosis, PRECAUTIONS: Information for Patients)

For patients at risk of thrombosis, do not exceed the recommended dose of GamaSTAN S/D. Ensure adequate hydration in patients before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity. (see PRECAUTIONS: Thrombosis, DOSAGE AND ADMINISTRATION)

Administer Gama**STAN** S/D cautiously to patients with a history of prior systemic allergic reactions following the administration of human immunoglobulin preparations.(9)

GamaSTAN S/D is made from human plasma. Because GamaSTAN S/D is made from human blood, it may carry a risk of transmitting infectious agents, e.g., viruses and theoretically, the Creutzfeldt-Jakob Disease (CJD) agent. No cases of transmission of viral diseases or CJD have ever been identified for GamaSTAN S/D. ALL infections suspected by a physician possibly to have been transmitted by this product should be reported by the physician or other healthcare provider to Grifols Therapeutics Inc. [1-800-520-2807].

PRECAUTIONS

General

Do not administer Immune Globulin (Human) subcutaneously or intravenously because of the potential for serious reactions (e.g., Renal Dysfunction/Failure/Hemolysis, Transfusion-Related Acute Lung Injury [TRALI]. Do not inject into a blood vessel.

Thrombosis

Thrombosis may occur following treatment with immune globulin products, including Gama**STAN** S/D.(15-17) Risk factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling central vascular catheters, hyperviscosity, and cardiovascular risk factors. Thrombosis may occur in the absence of known risk factors.

Consider baseline assessment of blood viscosity in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia/markedly high triacylglycerols (triglycerides), or monoclonal gammopathies. For patients at risk of thrombosis, do not exceed the recommended dose of Gama**STAN** S/D. Ensure adequate hydration in patients before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity. (see BOXED WARNING, PRECAUTIONS: Information for Patients, DOSAGE AND ADMINISTRATION)

Hypersensitivity

Do not perform skin tests. In most patients the intradermal injection of concentrated gamma globulin solution with its buffers causes a localized area of inflammation which can be misinterpreted as a positive allergic reaction. In actuality, this does not represent an allergy; rather, it is localized tissue irritation of a chemical nature. Misinterpretation of the results of such tests can lead the physician to withhold beneficial human immunoglobulin from a patient who is not actually allergic to this material.

Although true allergic responses to human gamma globulin given in the prescribed intramuscular manner are rare, have epinephrine available for treatment of acute allergic symptoms, should they occur.

Information for Patients

Thrombosis

Instruct patients to immediately report symptoms of thrombosis. These symptoms may include: pain and/or swelling of an arm or leg with warmth over the affected area, discoloration of an arm or leg, unexplained shortness of breath, chest pain or discomfort that worsens on deep breathing, unexplained rapid pulse, numbness or weakness on one side of the body.

Clinical and Laboratory Tests

None required.

Product Interactions

Passive transfer of antibodies may transiently impair the immune responses to live attenuated virus vaccines such as mumps, rubella and varicella for up to 6 months and for a year or more to measles (rubeola). Inform the immunizing physician of recent therapy with Gama**STAN** S/D so that appropriate precautions can be taken.

No interactions with other products are known.

Pregnancy Category C

Animal reproduction studies have not been conducted with Gama**STAN** S/D. It is also not known whether Gama**STAN** S/D can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Gama**STAN** S/D should be given to a pregnant woman only if clearly needed.

Pediatric Use

Safety and effectiveness in the pediatric population have not been established.

ADVERSE REACTIONS

Local pain and tenderness at the injection site, urticaria, and angioedema may occur. Anaphylactic reactions, although rare, have been reported following the injection of human immune globulin preparations.(6,9) Anaphylaxis is more likely to occur if Gama**STAN** S/D is given intravenously; therefore, Gama**STAN** S/D must be administered only intramuscularly.

DOSAGE AND ADMINISTRATION

- FOR INTRAMUSCULAR ADMINISTRATION ONLY.
- DO NOT ADMINISTER SUBCUTANEOUSLY OR INTRAVENOUSLY.

- Visually inspect parenteral drug products for particulate matter and discoloration prior to administration, whenever solution and container permit.
- Administer Gama**STAN** S/D **intramuscularly** (see PRECAUTIONS), preferably in the anterolateral aspects of the upper thigh and the deltoid muscle of the upper arm. Do not use the gluteal region as an injection site because of the risk of injury to the sciatic nerve.(10) Doses over 10 mL should be divided and injected into several muscle sites to reduce local pain and discomfort. An individual decision as to which muscle is injected must be made for each patient based on the volume of material to be administered.
- Draw back on the plunger of the syringe before injection in order to be certain that the needle is not in a blood vessel.
- A number of factors could reduce the efficacy of this product or even result in an ill effect following its use. These include improper storage and handling of the product after it leaves our hands, diagnosis, dosage, method of administration, and biological differences in individual patients. Because of these factors, it is important that this product be stored properly and that the directions be followed carefully during use.

Hepatitis A

Gama**STAN** S/D 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 Gama**STAN** S/D are recommended for persons who plan to travel in areas where hepatitis A is common.(3)

Length of Stay	**Dose Volume**
Less than 3 months	0.02 mL/kg
3 months or longer	0.06 mL/kg (repeat every 4–6 months)

Measles (Rubeola)

Give Gama**STAN** S/D in a dose of 0.11 mL/lb (0.25 mL/kg) to prevent or modify measles in a susceptible person exposed fewer than 6 days previously.(7)

To a susceptible child who is exposed to measles and who is immunocompromised, administer a dose of 0.5 mL/kg (maximum dose, 15 mL) of Gama**STAN** S/D immediately.(8)

Varicella

If Varicella-Zoster Immune Globulin (Human) is unavailable, Gama**STAN** S/D at a dose of 0.6 to 1.2 mL/kg, promptly given, may also modify varicella.(5) For patients at risk of thrombosis, administer Gama**STAN** S/D at the lower range of the recommended dose.

Rubella

Some studies suggest that the use of Gama**STAN** S/D in exposed, susceptible women can lessen the likelihood of infection and fetal damage; therefore, Gama**STAN** S/D at a dose of 0.55 mL/kg may benefit those women who will not consider a therapeutic abortion.(4)

HOW SUPPLIED

Gama**STAN** S/D is supplied in 2 mL and 10 mL single dose vials. Gama**STAN** S/D is preservative-free and latex-free.

NDC Number	Size
13533-635-02	2 mL vial (10 pack)
13533-635-04	2 mL vial
13533-635-10	10 mL vial (10 pack)
13533-635-12	10 mL vial

STORAGE

- Store at 2–8°C (36–46°F).
- Do not freeze.
- Do not use after expiration date.

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