For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory.

Antithymocyte Globulin-Equine
Thymogam

For I.V. use only

Description :
Thymogam is a sterile, transparent to slightly opalescent aqueous colourless to pale yellow solution containing Antithymocyte globulin. **Thymogam** is obtained by processing hyperimmune serum of horses immunized with human thymocytes.

Composition :
Each 5ml vial contains :
Antithymocyte Globulin (Equine) : 100mg / 250mg
Water for Injection I.P. ..... q.s.
Stabilizer : Glycine I.P.
Excipients : Sodium Chloride I.P.

Actions :
The immunosuppressive action of **Thymogam** is apparently due to its interactions with T lymphocytes that result in the clearance of the cells as manifested by loss of CD3+ and CD2+ lymphocytes from the circulating blood. The mechanisms for this clearance probably include both cytotoxicity of the antibody mediated by complement and clearing in the reticuloendothelialsystem due to macrophage extraction of the opsonized T lymphocytes.

Indications and Uses :
Renal transplantation : **Thymogam** is indicated for the management of allograft rejection, including delay of onset of first rejection episode, in patients who have undergone renal transplantation. It is also given as an adjunct along with the conventional therapy to delay the onset of 1st rejection episode.
Aplastic Anaemia : **Thymogam** is indicated in the treatment of moderate to severe aplastic anaemia in patients not suitable for bone marrow transplant.

Dosage and Administration :
Renal Allograft Recipients : 10 to 15mg/kg daily for 14 days (14 doses) followed by alternate day therapy for further 14 days (7 doses) bringing the total doses to 21 in 28 days.
In children, doses in the range of 5 to 25mg/kg daily have been administered and in adult renal allograft recipients doses of 10 to 30mg/kg daily have been administered. When given to delay onset of first rejection episode, start therapy within 24 hours before or after transplant. When given to treat rejection, start therapy at time of diagnosis of the first rejection episode.
Thymogam can also be used concomitantly with azathioprine and corticosteriods which are also used to suppress the immune response.
Aplastic Anaemia Recipients : 10 to 20mg/kg daily for 8-14 days followed by alternate day therapy for a total of 21 doses. These patients are to be monitored continuously for thrombocytopenia. When administered with a regime of supportive care it may induce partial to complete haematological remission.

Administration :
Thymogam should be diluted before use in 0.9% Sodium Chloride Injection, 5% Dextrose and 0.225% Sodium Chloride, or 5% Dextrose and 0.45% Sodium Chloride Injection to a concentration not to exceed 4mg of Antithymocyte Globulin per ml. The diluted solution should be gently rotated or swirled to effect thorough mixing and allowed to reach room temperature before infusion. **Thymogam** is appropriately administered into a vascular shunt, arterial venous fistula, or a high-flow central vein through an in-line

filter with a pore size of 0.2 to 1.0 micron. **Thymogam** once diluted has been shown to be physically and chemically stable for up to 24 hours at concentrations of upto 4mg/ml in the diluents recommended.
Adding **Thymogam** only to dextrose injection is not recommended, as a low salt concentrations can cause precipitation. Highly acidic infusion solutions can also contribute to physical instability over time. It is recommended that diluted **Thymogam** be stored in a refrigerator and be used within 24 hours.

Contraindications :
Thymogam should not be administered to a patient who has previous history of severe systemic reaction to this preparation or any other equine globulin preparations.

Warnings and Precautions :
Only physicians experienced in immunosuppressive therapy should use **Thymogam.** Use **Thymogam** only in facilities equipped and staffed with adequate laboratory and supportive medical resources. Discontinue therapy if anaphylaxis or severe and unremitting thrombocytopenia or leucopenia occurs. As observed with products derived from or purified with human blood components, the possibility of transmission of some infectious disseases should be borne in mind. Monitor patients carefully for concurrent infection. Several studies have suggested and increase in the incidence of cytomegalovirus infection in patients receiving **Thymogam**. To identify those at greatest risk of systemic anaphylaxis, physician should strongly recommend skin testing before commencing treatment. A conservative, conventional approach would first employ epicutaneous (prick) testing with undiluted **Thymogam**. If the subject does not show a wheal ten minutes after pricking, proceed to intradermal testing with 0.02mL of a 1:1000 dilution of **Thymogam** in Sodium chloride injection with a separate Sodium chloride injection control of similar volume. Observe the results every 10 minutes over the first hour after intradermal injection. A wheal of 3mm or greater in diameter at the site of **Thymogam** injection than that at the Sodium chloride injection control site (or a positive prick test) shows clinical sensitivity and an increased possibility of systemic allergic reactions.

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Note :
The predictive value of this test has not been proved clinically. Allergic reactions such as anaphylaxis have occurred in patients whose skin test is negative. In the presence of a locally positive skin test to **Thymogam**, serious consideration to alternative forms of therapy should be given.
A systemic reaction such as a generalized rash, tachycardia, dyspnea, hypotension, or anaphylaxis precludes any additional administration of **Thymogam**.

Use during pregnancy and lactation :
Thymogam has not been evaluated in either pregnant or lactating women. Animal reproduction studies have not been conducted with **Thymogam.** It is also not known whether **Thymogam** can cause foetal harm when administered to a pregnant woman or can affect reproduction capacity. **Thymogam** administration to pregnant women is not recommended and should be considered only under exceptional circumstances. It is not known whether **Thymogam** is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from **Thymogam**, caution should be exercised when **Thymogam** is administered to a nursing woman.

Adverse Effects :
Renal Transplantation : The primary clinical experience with **Thymogam** has been in renal allograft patients receiving concurrent standard immunosuppressive treatment. In these patients, investigators have most frequently reported fever, chills, leucopenia, thrombocytopenia, arthralgia and dermatologic reactions such as rash, urticaria, wheal, flare and pruritis.
Aplastic Anaemia : The incidence of adverse reaction has been found more in patients being treated for aplastic anaemia. Frequently reported adverse reactions among patients enrolled in aplastic anaemia

studies were fever, chills, skin rashes, arthralgia and thrombocytopenia. In patients with aplastic anaemia and other haematologic abnormalities who have received **Thymogam**, abnormal tests of liver function (SGOT, SGPT, alkaline phosphatase) and renal function (serum creatinine) have been observed. In some trials, clinical and laboratory findings of serum sickness have been in majority of patients.
Other Reactions : Other reactions reported are : headache, nausea, vomiting, diarrhoea, dyspnoea, hypotension, night sweats, stomatitis, chest pain, back pain, pain at the infusion site, clotted A/V fistula and peripheral thrombophlebitis. Reactions reported rarely are : periorbital oedema, agitation, dizziness, weakness or faintness, malaise, epigastric pain or hiccoughs, laryngospasm, paraesthesia, lymphadenopathy, infection, possible encephalitis, herpes simplex reactivation, wound dehiscence, hyperglycaemia, hypertension, oedema, pulmonary oedema, pleural effusions, tachycardia, seizure, anaphylaxis, iliac vein obstruction, renal artery thrombosis, proteinuria and toxic epidermal necrosis.

Interactions :
When the dose of corticosteroids and other immunosuppressants is being reduced, some previously masked reactions toThymogam may appear. Under these circumstances, observe patients especially carefully during therapy with **Thymogam**.

Overdosage :
Because of its mode of action and because it is a biological substance, the maximal tolerated dose of **Thymogam** would be expected to vary from patient to patient. To date, the largest single daily dose administered to a patient, a renal transplant recipient, was 7000mg administered at a concentration of approximately 10mg/ml diluted with Sodium Chloride Injection, USP, approximately 7 times the recommended total dose and infusion concentration.
The maximum number of doses (10 to 20 mg/kg/dose) that can be administered ot a single patient has not yet been determined. Some renal transplant patients have received up to 50 doses in 4 months, and others have received 28-day courses of 21 doses followed by as many as 3 more courses for the treatment of acute rejection. The incidence of toxicological manifestations did not increase with any of these regimens.

Storage condition :
Store between 2^0C and 8^0C. Do not freeze.

Presentation :
Thymogam is available in vial packs, each vial (5ml) containing 100mg / 250mg of Antithymocyte Globulin (equine).

Manufactured in India by :
BHARAT SERUMS AND VACCINES LIMITED
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