Human Normal Immunoglobulin IP 5%

IVNEX™ आइवीनेक्स

Composition:
Each Vial contains:

Human Immunoglobulin	50 g/Lit
Maltose	100 g/Lit
Water for injection	q.s.

DESCRIPTION
IVNEX™ Solution is a sterile, non-pyrogenic preparation of human normal immunoglobulin g in a single dosage form for intravenous administration. Each 100ml contains 5g of human normal immunoglobulin and is prepared from qualified human plasma using membrane filtered and combination of chromatographic steps and viral inactivation steps.
The manufacturing process uses plasma collected from the donors who are screened for their history as per guidelines laid down by the regulatory authorities. Their blood is screened for the mandatory infectious diseases. Only on being declared negative to HbsAg, HCV and HIV antibodies the plasma is used for processing.

CLINICAL PHARMACOLOGY
IVNEX™, Human Normal Immunoglobulin Intravenous, contains a broad spectrum of IgG antibodies against bacterial and viral agents that are capable of opsonization and neutralization of microbes and toxins. Peak levels of IgG are reached immediately after infusion of IVNEX™. It has been shown that, after infusion, exogenous IgG is distributed relatively rapidly between plasma and extravascular fluid until approximately half is partitioned in the extravascular space. Therefore, a rapid initial drop in serum IgG levels is to be expected. As a class, it is reported that IgG survives longer *in vivo* than other serum proteins.

INDICATIONS AND USAGE
- **Primary Immunodeficiency Diseases**
  IVNEX™ is indicated for the treatment of primary immunodeficient states, such as: congenital agammaglobulinemia, common variable immunodeficiency, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies.
- **B-cell Chronic Lymphocytic Leukemia (CLL)**
- IVNEX™ is indicated for prevention of bacterial infections in patients with hypogammaglobulinemia and/or recurrent bacterial infections associated with B-cell Chronic Lymphocytic Leukemia (CLL).
- **Idiopathic Thrombocytopenic Purpura (ITP)**
  IVNEX™ is indicated when a rapid rise in platelet count is needed to prevent and/or to control bleeding in a patient with Idiopathic Thrombocytopenic Purpura.
- **Kawasaki Syndrome**
  IVNEX™ is indicated for the prevention of coronary artery aneurysms associated with Kawasaki syndrome.
- **Guillian Barre Syndrome**
  IVNEX™ is used as an immunomodulator therapy in Guillian Barre Syndrome

CONTRAINDICATIONS
IVNEX™ is contraindicated in patients with selective IgA deficiency where the IgA deficiency is the only abnormality of concern. Patients may experience severe hypersensitivity reactions or anaphylaxis in the setting of detectable IgA levels following infusion of IVNEX™. The occurrence of severe hypersensitivity reactions or anaphylaxis under such conditions should prompt consideration of an alternative therapy.

IVNEX™ , Human Normal Immunoglobulin Intravenous, is made from human plasma. Products made from human plasma may contain infectious agents, such as viruses, that can cause disease. The risk that such products will transmit an infectious agent has been reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain current virus infections, and by inactivating and/or removing certain viruses. Despite these measures, such products can still potentially transmit disease. Because this product 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.

IVNEX™, Human Normal Immunoglobulin Intravenous, should only be administered intravenously. Other routes of administration have not been evaluated. Immediate anaphylactic and hypersensitivity reactions are a remote possibility. Epinephrine and antihistamines should be available for treatment of any acute anaphylactoid reactions.

PRECAUTIONS
Hypersensitivity
Severe hypersensitivity reactions may occur. In case of hypersensitivity, discontinue IVNEX™ infusion immediately and institute appropriate treatment. Medications such as epinephrine should be available for immediate treatment of acute hypersensitivity reactions.

Renal Dysfunction/Failure
Acute renal dysfunction/failure, osmotic nephropathy, and death may occur upon use of human IVIg products. Ensure that patients are not volume depleted before administering IVNEX™ **In patients who are at risk of developing renal dysfunction, because of pre-existing renal insufficiency or predisposition to acute renal failure (such as diabetes mellitus, hypovolemia, overweight, use of concomitant nephrotoxic medicinal products or age of >65 years), administer IVNEX™ at the minimum infusion rate.**

Hyperproteinemia, Increased Serum Viscosity, and Hyponatremia
Hyperproteinemia, increased serum viscosity, and hyponatremia may occur in patients receiving IVIg therapy. It is critical to clinically distinguish true hyponatremia from a pseudohyponatremia that is associated with or causally related to hyperproteinemia with concomitant decreased calculated serum osmolality or elevated osmolar gap, because treatment aimed at decreasing serum free water in patients with pseudohyponatremia may lead to volume depletion, a further increase in serum viscosity, and a possible predisposition to thrombotic events.

Thrombotic Events
Thrombotic events may occur following treatment with IVNEX™ and other IVIg products. Patients at risk include those with a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, coagulation disorders, prolonged periods of immobilization, and/or known/suspected hyperviscosity. **For patients judged to be at risk of developing thrombotic events, administer IVNEX™ at the minimum rate of infusion.**

Aseptic Meningitis Syndrome (AMS)
AMS may occur infrequently with IVIg treatment. AMS usually begins within several hours to 2 days following IVIg treatment. Discontinuation of IVIg treatment has resulted in remission of AMS within several days without sequelae. AMS may occur more frequently in association with high doses (2 g/kg) and/or rapid infusion of IVIg.

Hemolysis
IVIg products can contain blood group antibodies that may act as hemolysins and induce *in vivo* coating of red blood cells (RBCs) with immunoglobulin, causing a positive direct antiglobulin reaction and, rarely, hemolysis. Delayed hemolytic anemia can develop subsequent to IVIg therapy due to enhanced RBC sequestration and acute hemolysis, consistent with intravascular hemolysis, has been reported.

Transfusion-related Acute Lung Injury (TRALI)
Noncardiogenic pulmonary edema may occur in patients following IVIg treatment. TRALI is characterized by severe respiratory distress, pulmonary edema, hypoxemia, normal left ventricular function, and fever. Symptoms typically appear within 1 to 6 hours following treatment. Monitor patients for pulmonary adverse reactions. If TRALI is suspected, perform appropriate tests for the presence of anti-neutrophil antibodies in both the product and the patient's serum. TRALI may be managed using oxygen therapy with adequate ventilatory support.

Transmissible Infectious Agents
IVNEX™ is made from human plasma. Based on effective donor screening and product manufacturing processes, IVNEX™ carries an extremely remote risk of transmission of viral diseases. A theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD) also is considered to be extremely remote.

Monitoring: Laboratory Tests
- Periodic monitoring of renal function and urine output is particularly important in patients judged to be at increased risk of developing acute renal failure. Assess renal function, including measurement of BUN and serum creatinine, before the initial infusion of IVNEX™ and at appropriate intervals thereafter.
- Because of the potentially increased risk of thrombosis, 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.
- If signs and/or symptoms of hemolysis are present after an infusion of IVNEX™, perform appropriate laboratory testing for confirmation.
- If TRALI is suspected, perform appropriate tests for the presence of anti-neutrophil antibodies in both the product and patient's serum.

Information For Patients
Patients should be instructed to immediately report symptoms of decreased urine output, sudden weight gain, fluid retention/edema, and/or shortness of breath (which may suggest kidney damage) to their physician.
Pregnancy Category C
Animal reproduction studies have not been conducted with IVNEX™. It is also not known whether IVNEX™ can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. IVNEX™ should be given to a pregnant woman only if clearly needed.

ADVERSE REACTIONS
The following is a list of adverse reactions that have been identified and reported during the post-approval use of IVIg products:

Infusion reactions: Hypersensitivity (e.g., anaphylaxis), headache, diarrhea, tachycardia, fever, fatigue, dizziness, malaise, chills, flushing, urticaria or other skin reactions, wheezing or other chest discomfort, nausea, vomiting, rigors, back pain, myalgia, arthralgia, and changes in blood pressure

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Renal: Acute renal dysfunction/failure, osmotic nephropathy

Respiratory: Apnea, Acute Respiratory Distress Syndrome (ARDS), TRALI, cyanosis, hypoxemia, pulmonary edema, dyspnea, bronchospasm

Cardiovascular: Cardiac arrest, thromboembolism, vascular collapse, hypotension

Neurological: Coma, loss of consciousness, seizures, tremor, aseptic meningitis syndrome

Integumentary: Stevens-Johnson syndrome, epidermolysis, erythema multiforme, dermatitis (e.g., bullous dermatitis)

Hematologic: Pancytopenia, leukopenia, hemolysis, positive direct antiglobulin (Coombs') test

Gastrointestinal: Hepatic dysfunction, abdominal pain

General/Body as a Whole: Pyrexia, rigors

DOSAGE AND ADMINISTRATION

For Intravenous Use Only
Preparation and Handling
- IVNEX™ is a clear or slightly opalescent, colorless solution. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use if the solution is cloudy or turbid, or if it contains particulate matter.
- Do not freeze, and do not use any solution that has been frozen.
- DO NOT SHAKE.
- IVNEX™should be at room temperature at the time of administration.
- Do not use IVNEX™ beyond the expiration date on the product label.
- The IVNEX™ is for single use only. Dispose of partially used or unused product.
- **Infuse IVNEX™ using a separate infusion line.**
  Do not mix with other intravenous medications (including normal saline) or other IVIg products.

DOSAGE
As there are significant differences in the half-life of IgG among patients with Primary Immunodeficiency, the frequency and amount of immunoglobulin therapy may vary from patient to patient. The proper amount can be determined by monitoring clinical response.

The recommended dose of IVIg for patients with Primary Immunodeficiency is 300 to 600 mg/kg administered every 3 to 4 weeks. Adjust the dosage over time to achieve the desired serum trough levels and clinical responses. If a patient misses a dose, administer the missed dose as soon as possible, and then resume scheduled treatments every 3 or 4 weeks, as applicable.

Idiopathic Thrombocytopenic Purpura (ITP)
The usual dosage for the treatment of acute and chronic ITP is 200-400 mg/kg daily given for 5 consecutive days. The additional doses are discontinued if an adequate response does not occur.

Kawasaki Syndrome
The usual dosage is 400 mg/kg daily for 5 consecutive days.

Infusion rate
0.01 - 0.02 mL/kg/min for the first 30 minutes and increase upto 0.06 mL/kg/min if there are no adverse effects.

Guillian Barre Syndrome : The dose in Guillain-Barré syndrome is 0.4 g/kg/day for 5 days.

Storage
Store between 2°C to 8°C. Do not freeze. Protect from light.
Keep out of reach of children.

How Supplied
IVNEX™ is available as 5000 mg/100 mL vial.

Shelf life: Please refer to carton/label.

Special precautions for disposal and other handling
IVNEX™ solutions must not be diluted with water for injections as this may cause haemolysis in recipients.
Any unused medicinal product or waste material should be disposed of in accordance with local regulatory requirements

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To report adverse events and/or product complaints visit our website **www.biocon.com** or call toll free No: **1800 102 9465** or e-mail us at **drugsafety@biocon.com**