

Leaflet text for Normoglobin™

Human Normal Immunoglobulin BP



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Presentation:

Normoglobin™: Each vial contains 10 ml human normal immunoglobulin BP containing \geq 500 mg of human immunoglobulin-G (IgG).

Normoglobin™ 2.5: Each vial contains 50 ml human normal immunoglobulin BP containing \geq 2500 mg of human immunoglobulin-G (IgG).

Description

Normoglobin is a ready to use, sterile, clear or slightly opalescent and colorless to pale yellow, liquid preparation of purified immunoglobulin-G (IgG) obtained from human plasma pools. The purification processes include thawing, cold ethanol fractionation, chromatography, virus inactivation with S/D fractionation and nano-filtration and dia-filtration. The final bulk is manufactured by adding maltose (as stabilizer) to bulk product and passing through sterile filter, after this the final bulk is filled into vials.

Indications and uses

IMMUNOMODULATION THERAPY

- Idiopathic Thrombocytopenic Purpura (ITP)
- Guillain Barre Syndrome (GBS)
- Kawasaki disease
- CIDP (Chronic Inflammatory Demyelinating Polyneuropathy)
- General myopathy
- Wegener granulomatosis
- Dermatomyositis
- Systemic connective tissue disease (Rheumatoid arthritis)

REPLACEMENT THERAPY

Primary immunodeficiency syndrome such as

- Congenital agammaglobulinemia and hypogammaglobulinemia
- Common variable immunodeficiency
- Severe combined immunodeficiency
- Wiskott-Aldrich syndrome
- Transient hypogammaglobulinemia in

Secondary immunodeficiency syndrome such as

- Cytopenia of different origin (acute and chronic leukemia, aplastic anemia, condition after cytostatic therapy)
- Severe forms of bacterial-toxic and viral infections in adults and children (including surgical complications accompanied by bacteremia and septicopyemic conditions and in preparation of surgical patients to surgery)
- Prophylaxis and treatment of infections in premature infants with low birth weight
- Severe recurrent bacterial infection in children with HIV/AIDS

Dosage and administration

- For Idiopathic Thrombocytopenic Purpura: During 2-5 days 4-8 ml (200-400 mg)/kg daily or 16-20 ml (0.8 – 1) g/kg on day 1, if necessary on day 3.
- For Guillain-Barré syndrome, chronic inflammatory neuropathy (myelin sheath decomposition), general myopathy, Wegener granulomatosis: 8 ml (0.4 g)/kg/day during 3-7 days, if necessary, 5-day treatment courses may be repeated with 4-week intervals.
- Kawasaki syndrome: 20-40 ml (1-2 g)/kg in equal doses for 2-5 days or 40 ml (2 g)/kg in a single dose (supplement to acetylsalicylic acid therapy).
- During congenital agammaglobulinemia or hypogammaglobulinemia and other syndromes of primary deficiency (including severe combined immunodeficiency, Wiskott-Oldrich syndrome, common variable immunodeficiency, transient hypogammaglobulinemia) in children: 8-10 ml (0.4-0.5 g)/kg (minimum dose 4 ml (0.2 g)/kg, maximum dose 16 ml (0.8 g)/kg) every 3-4 weeks, the dose selection to be made individually depending on the severity of the infectious syndrome (serum IgG of 5 g/l is considered optimal, but not less than 3-4 g/l).
- Replacement therapy in secondary immunodeficiencies: 4-8 ml (0.2-0.4 g)/kg every 3-4 weeks.
- Severe recurrent bacterial infections in children with HIV/AIDS: 8 ml (0.4 g)/kg every 3-4 weeks
- Different origins Cytopenia (acute and chronic leukemia, aplastic anemia, condition after cytotoxic therapy): 4-8 ml (0.2-0.4g)/kg/day during 4-5 days or 20 ml (1 g)/kg/day during 2 days.
- Severe forms of bacterial-toxic and viral infections in adults and children (including surgical complications, accompanied by bacteremia and septicopyemic conditions and in the preparation for surgical patients to surgery): 8 ml (0.4 g)/kg/day during 1-4 days
- During allogeneic bone marrow transplantation: 4-8 ml (0.2-0.4 g)/kg/day every 3-4 weeks till the clinical tests of IgG levels will stabilize. If necessary dosage can be increased to 10 ml (0.5 g)/kg.
- Dermatomyositis: 20 ml (1 g)/kg/day during 3-5 days.
- Systemic connective tissue diseases (rheumatoid arthritis): 4-10 ml (0.2-0.5 g)/kg/day during 5 days
- Prophylaxis and treatment of premature infants infections with low birth weight: 3-8 ml (0.15- 0.4 g)/kg on day 2 or 3 of life (at the first stage) and on week 2 or 3 of life (at the second stage).

Children: Human Normal Immunoglobulin can also be used for pediatric purpose according to the above dose.

Method of administration

The human normal immunoglobulin is for intravenous use only. The product should be warmed to room or body temperature before use. The human normal immunoglobulin should be infused intravenously at the following rates:

The infusion rate for children is 0.08-0.5 ml/min depending on the body weight. For adults, the infusion rate is 1-1.5 ml/min. More rapid administration may cause colloid reaction.

Precautions

- Product should be maintained at a temperature of (20±2) °C for at least 2 hours' prior infusion.
- The solution should be clear to slightly opalescent, colorless to slightly yellowish. Do not use solutions that are cloudy or have deposits.
- The human normal immunoglobulin is manufactured from human plasma and it has the potential to transmit hepatitis viruses or other viruses which can cause infection. The risk of virus infection cannot be entirely eliminated. Accordingly, patients with hemophilia or immunodeficiency are recommended to be appropriately vaccinated (Hepatitis A vaccine, etc.), and the attending physician should monitor patients regularly to check any sign of virus infection. Since human normal immunoglobulin has potential risks as described above, the product must be carefully used. If the product is prescribed, only the necessary amount should be administered.
- The risk of thrombosis by administration of this product cannot be entirely eliminated. Thrombosis may occur regardless of the route of administration and in the absence of known risk factors (advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling central vascular catheters, hyperviscosity and cardiovascular risk factors). For patients at risk of thrombosis, administer at the minimum concentration possible and at the minimum rate of infusion practicable. Also ensure adequate hydration in patients before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity.

Special precautions:

- Severe hypersensitivity reactions and anaphylactic reactions with a fall in blood pressure may occur. Patients with antibodies to IgA have a greater risk of developing potentially severe hypersensitivity and anaphylactic reactions.
- Patients with renal disorder (Renal function may deteriorate), acute renal dysfunction/failure, acute tubular necrosis, proximal tubular nephropathy, osmotic nephrosis and death have been reported in patients receiving IVIG. It should be ensured that patients are not volume-depleted before administration of the IVIG. For patients judged to be at risk for developing renal dysfunction, including patients with any degree of pre-existing renal insufficiency, diabetes mellitus, age greater than 65, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs, IVIG should be administered at the minimum dose and rate of infusion practicable.
- Patients with hemolytic anemia or anemia from blood loss (Human parvovirus B19 infection may occur. In case of infection, acute systemic symptoms with fever and severe anemia may occur.)
- Patients with immunological incompetence or immunodeficiency (Human parvovirus B19 infection may occur. In case of infection, continuous anemia may occur.)
- Patients with cerebrovascular and cardiovascular disorders or case history thereof for example, (Elderly patients with ischemic disease, cardiovascular disorder, cerebrovascular disorders or case of history thereof: a large bolus administration can cause thrombus or embolism such as cerebral infarction, a myocardial infarction, etc. due to blood viscosity increase.)
- Patients with high risk of thrombus or embolism (Thrombus or embolism may occur due to an increase of blood viscosity due to large bolus administration.)
- Patients with low heart function. (A large bolus administration may cause heart failure or deterioration of heart condition.)

- Patients should take caution with IgA deficiency. (IVIg may cause anaphylaxis to patients who have anti-IgA)
- Aseptic Meningitis Syndrome (AMS) has been reported to occur following high dose (e.g. over 1.0 g per kg body weight) of IVIG treatment or rapid infusion of IVIG. The symptoms of AMS usually begin 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 is characterized by the following signs and symptoms: severe headache, nuchal rigidity, drowsiness, fever, photophobia, painful eye movements, nausea and vomiting.
- Human normal immunoglobulin may contain blood group antibodies that may act as hemolysins and induce in vivo coating of red blood cells with immunoglobulin, causing a positive direct antiglobulin test result and hemolysis. Delayed hemolytic anemia can develop subsequent to IVIG therapy due to enhanced red blood cell sequestration and acute hemolysis, consistent with intravascular hemolysis, has been reported.
- Non-cardiogenic pulmonary edema has been reported in patients following IVIG treatment. Transfusion-related acute lung injury is characterized by severe respiratory distress, pulmonary edema, hypoxemia, normal left ventricular function and fever. Symptoms typically appear within 1 to 6 hours after transfusion.

General cautions:

- In case of successive or interval administration, shock or severe abnormal reactions may occur. Accordingly, administration should be done with caution, and catamnesis also should be carefully observed. Especially for children, special caution should be taken for the rate of administration and catamnesis.
- Administration of human normal immunoglobulin for the treatment of Idiopathic Thrombocytopenic Purpura is for symptomatic therapy, not causal treatment.
In case of Idiopathic Thrombocytopenic Purpura for children, spontaneous remission should be considered.
In present plasma fractionation process, it is difficult to inactivate or remove human parvovirus B19 etc. completely.
- Accordingly, possibilities of infection cannot be disregarded, and special caution should be taken for catamnesis.
- Even though a safety plan for the prevention of the spread of infection is prepared, the risk of infection cannot be entirely disregarded since human normal immunoglobulin originates from human blood. This risk should be explained to patients.
- Since human normal immunoglobulin contains anti-A and anti-B, hemolytic anemia may occur when a large bolus is administered to patients with blood type A, B or AB.
In the case of combined therapy with antibiotics in severe infections, human normal immunoglobulin should be used for patients who show insufficient response to proper antimicrobial chemotherapy.
- There have been published reports that immune globulin intravenous injection is related to disorders of renal function, osmotic renal diseases, including death etc.
- Additional administration to patients with Kawasaki Syndrome should be conducted when the effectiveness of immunoglobulin is insufficient (e.g. symptomatic remission) or additional administration is clearly necessary. (Safety and efficacy for additional administration has not been established)
- Patients should be aware of the risk and discuss with their healthcare professionals and contact them if any signs or symptoms of thrombosis during or after receiving this product develop.
- Healthcare professionals should be aware of the risk for thrombosis with human normal immunoglobulin products and discuss with their patients the risk of thrombosis associated with this product. Monitor patients carefully for signs and symptoms of thrombosis both at the time of infusion and after infusion and encourage patients to report any signs or symptoms.

Special precautions for disposal and other handling precautions for administration

- Avoid mixing with other medicinal products except for 5%-Glucose. (Do not mix with normal saline)
- Rapid administration may cause hypotension. Drip infusion intravenous injection is recommendable. If direct intravenous injection is needed, it should be administered very slowly. (Caution should be taken with A-/Hypogammaglobulinemia patients.)
- If particulate matter is observed, or color is not clear, the product should be discarded.
- Human normal immunoglobulin should be used within 1 hour after the container is opened. Do not use the remaining solution due to the possibility of microbial contamination. (Human normal immunoglobulin is protein and does not contain preservatives.)
- Do not use if human normal immunoglobulin was ever frozen.
- When a needle is inserted through the rubber stopper, the needle should be inserted vertically and slowly. If a needle is inserted in a tilted or twisted direction, rubber fragments may be mixed with medicinal product. If there are any rubber fragments, discard the product.

Contraindications

- Contraindicated in patients who have had a history of anaphylactic or severe systemic hypersensitivity reactions to the administration of human normal immunoglobulin.
- This product is also contraindicated in IgA deficient patients with antibodies to IgA and a history of hypersensitivity.

Co-Administration

- There is a possibility that live vaccines (measles, mumps, rubella and varicella vaccine etc.) do not work for the patients who were treated with human normal immunoglobulin. Therefore vaccination should be delayed for 3 months after administration. If human normal immunoglobulin is administered within 14 days after vaccination, re-vaccination should be taken after more than 3 months of post administration.
- After a large bolus (more than 200 mg/kg) administration for the ITP and Kawasaki disease, use of live vaccines should be delayed more than 6 months. In case of low risk of measles infection, measles vaccination can be delayed for more than 11 months.

Use in specific population

Pregnancy: Safety for a pregnant woman has not been established. The possibility of parvovirus B-19 infection cannot be excluded from the administration of human normal immunoglobulin. In case of parvovirus B-19 infection, fetal disturbances (Abortion, Hydrops fetalis, fetal death) may occur. Human normal immunoglobulin should be given to a pregnant woman only if the expected benefit justifies the possible risk.

Lactation: Use of this product has not been evaluated in nursing mothers.

Pediatric: Children may be more susceptible to fluid overload.

Geriatric: Since elderly patients generally have low physiological function, human normal immunoglobulin should be administered with special care.

Influence to clinical examination results

Human normal immunoglobulin contains pathogens or antibodies against the pathogens. Therefore, antibodies can be occasionally detected in blood after administration. Clinical diagnosis should be taken with special cautions and confirmed.

Side effects

- Symptoms of shock may occur. If dyspnea, wheeze, chest pain, hypotension or weak pulse are watched, administration should be discontinued and 0.1-0.5 ml epinephrine (1:1000) or the administration of cortisone should be considered.
- Rapid administration can cause hypotension.
- Liver function disorders or jaundice accompanying and increase in ALT or AST may occur. Caution should be taken and proper treatment should be followed if needed.
- Renal failure may occur with the use of human normal immunoglobulin. If dehydration, hypourisemia, increase of creatinine or increase of BUN etc is observed, administration should be discontinued and proper treatment should be taken.
- Aseptic meningitis from a large volume of human normal immunoglobulin administration (Nuchal rigidity, fever, headache, nausea, vomiting, mental fog, etc.) may occur. In these cases, administration should be discontinued and proper treatment taken.
- Decrease in platelets may occur. Caution should be taken. If this symptom occurs, proper treatment should be taken
Other possible undesirable effects include drowsiness, chill, chest pain, abdominal pain, gluteal pain and anxiety etc.

Overdose

Overdose may lead to fluid overload and hyperviscosity. Patients at particular risk of complications of fluid overload and hyperviscosity include elderly patients and patients with cardiac or renal impairment.

Storage

- Store and transport at +2 °C to +8 °C
- Protect from light
- Do not freeze
- Keep out of the reach and sight of children

Commercial Pack

Normogloblin : Each box contains 1 vial containing the human normal immunoglobulin BP.

Normogloblin 2.5: Each box contains 1 vial containing the human normal immunoglobulin BP and an infusion set.