Summary of Product Characteristics

1. Name of the medicinal product

Normoglobin
Human Normal Immunoglobulin BP; 5%
Normoglobin for intravenous use

2. Qualitative and quantitative composition

After reconstitution, each 1 ml contains ≥ 50 ml, human Immunoglobulin-G
For the full list of excipients, (see section 6.1)

3. Pharmaceutical form

Solution for Intravenous use

4. Clinical particulars

4.1 Therapeutic indications

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 children

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 surgicial 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

4.2 Posology and method of administration

4.2.1 Posology

- **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, Wiscott-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 (0.2-0.4 g)/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 septycopiyemical 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).

4.2.2 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 collaptoid reaction.

4.3 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.

4.4 Special warnings and precautions for use

- 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.

- 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 there of 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.

4.5 Interaction with other medical products and forms of interaction

- 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.

4.6 Fertility, pregnancy and lactation

4.6.1 In 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.

4.6.2 Breast-feeding

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

4.7 Effects on ability to drive and use machines

Some of the effects mentioned under section 4.8" Undesirable Effects" may affect the ability to drive or use machines.

4.8 Undesirable 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, hypouresis, 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.

4.9 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.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Human normal immunoglobulin contains the IgG antibodies present in the normal population. It is usually prepared from pooled plasma from not fewer than 1000 donations. It has a distribution of immunoglobulin G subclasses closely proportional to that in native human plasma. Adequate doses of this medicinal product may restore abnormally low immunoglobulin G levels to the normal range.

The mechanism of action in indications other than replacement therapy is not fully elucidated, but includes immunomodulatory effects

5.2 Pharmacokinetic properties

Human normal immunoglobulin is immediately and completely bioavailable in the recipient's circulation after intravenous administration. It is distributed relatively rapidly between plasma and extravascular fluid, after approximately 3-5 days' equilibrium is reached between the intra- and extravascular compartments.

The half-life may vary from patient to patient, in particular in primary immunodeficiency.

IgG and IgG-complexes are broken down in cells of the reticuloendothelial system

5.3 Preclinical safety data

There is no data or study on Intravenous Immunoglobulin., but clinical experience provides no toxicity or abnormal safety issue on this product.

6. Pharmaceutical particulars

6.1 List of excipients

Maltose
Water for injection

6.2 Incompatibilities

The vaccine must not be mixed with other medicinal products.

6.3 Shelf life

2 years when stored at +2 °C to +8 °C

6.4 Special precautions for 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

6.5 Nature and contents of container

- 10 ml (500 mg) in 10 ml vial (type I Borosilicate vial, type I Chlorobutyl rubber stopper)
- 50ml (2500mg) in a 50ml vial (type I Borosilicate vial, type I Chlorobutyl rubber stopper) with infusion set

6.6 Special precautions for disposal and other handling

- 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.

7. Marketing authorization holder

Incepta Pharmaceuticals Limited
Vaccine Division
Savar, Dhaka,
Bangladesh

8. Drug authorization number

Normoglobin 10ml: 363-24-069

Normoglobin 50ml: 363-32-069

9. Date of first authorization/Renewal of the authorization

Normoglobin 10ml: 24-Nov-2016

Normoglobin 50ml: 05-May-2019

10. Date of revision of the text

Normoglobin 10ml: 23-Nov-2026

Normoglobin 50ml: 04-May-2024