PACKAGE INSERT

1. NAME OF THE MEDICINAL PRODUCT

I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection.

2. QUANTITATIVE COMPOSITION

1 mL contains:
Human Immunoglobulin-G (Active ingredient) ---------- 100mg
(Human Normal Immunoglobulin for Intravenous Administration, 10%)
Glycine (Stabilizer) ----------18.8mg
Water for injection (Solvent) ----------q.s.

Each vial of 25 mL contains: 2,500 mg of human normal immunoglobulin G

This product I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection (Human Normal Immunoglobulin with glycine, pH 4.8', as a biological product is manufactured with plasma which was collected for the purpose of manufacture of plasma derivatives from individual donors. All plasma processes thawing, cold ethanol fractionation and virus inactivation processes such as S/D treatment and nano-filtration. Fraction II which comes from plasma fractionation is purified with chromatography, and takes S/D treatment for virus inactivation. After another purification process with chromatography is taken, dia-filtration is conducted. Nano-filtration process follows in order to remove viruses and bulk product is produced. Final bulk is manufactured by adding glycine (as stabilizer) to bulk product and passing through sterile filter, after this final bulk is filled into vials.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear or slightly turbid and colorless or pale yellow liquid.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

1) A-/Hypogammaglobulinemia
2) Combined therapy with antibiotics in severe bacterial or viral infections.
3) Idiopathic Thrombocytopenic Purpura (In the case where other medicinal products are not effective or patients show apparent hemorrhage or patients need temporary control of hemostasis such as surgeon treatments or childbirth etc.)
4) Guillain-Barre Syndrome (Subacute febrile polyneuritis)
5) Kawasaki Syndrome (To prevent the disease of coronary artery complication)

4.2 Posology and method of administration

1) For Combined therapy with antibiotics in severe bacterial or viral infections and A-/Hypogammaglobulinemia. The usual dosage for adults and children is 2,500-5,000 mg and 50-150 mg/kg respectively (as a single dose) by intravenous drip infusion or direct intravenous infusion. In case of intravenous injection, it should be injected very slowly.
2) Idiopathic Thrombocytopenic Purpura
The usual dosage for the treatment of acute or 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.
3) Guillain-Barre Syndrome

The usual dosage is 400 mg/kg daily given for 5 consecutive days.
4) Kawasaki Syndrome
The usual dosage is 400 mg/kg daily given for 5 consecutive days(approximately), or 2,000mg daily by intravenous drip infusion. It is recommended that the administration of I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection starts within 7 days from the onset of Kawasaki Syndrome.

4.3 Contraindications
1) Patients with history of hypersensitivity to ingredients of this product.
2) Patients with history of shock to ingredients of this product.

4.4 Special warnings and precautions for use
4.4.1 Special warnings
1) I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection manufactured from human plasma, has the potential to transmit hepatitis viruses or other transmissible agent 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 I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection has potential risks as described above, the patient should be fully informed at the time of administration, and should only use the minimum necessary after careful consideration of the therapeutic need.
2) 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.

4.4.2 Special precautions
1) Patients with IgA deficiency (I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection may cause anaphylaxis to patients who have anti-IgA)
2) Patients with renal disorder (Renal function may deteriorate.)
3) Patients with hemolytic anemia or anemia from blood loss (Human parvovirus B19 infection may occur. In case of B19 infection, acute systemic symptoms with fever and severe anemia may occur.)
4) Patients with immunological incompetence or immunodeficiency (Human parvovirus B19 infection may occur. In case of infection, continuous anemia may occur.)
5) Patients with cerebrovascular and cardiovascular disorders or case history thereof for example, (Elderly patients with ischemic disease, cardiovascular disorder, cerebrovascular disorder; or patients with cerebrovascular and cardiovascular disorders or case history thereof: a large bolus administration can cause thrombus or embolism such as cerebral infarction, a myocardial infarction, etc., due to blood viscosity increase.)
6) 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)
7) Patients with low heart function (A large bolus administration may cause heart failure or deterioration of heart condition)

4.4.3 General cautions
1) 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.
2) Administration of I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection for the treatment of Idiopathic Thrombocytopenic Purpura is for symptomatic therapy, not causal treatment.
3) In case of Acute Idiopathic Thrombocytopenic Purpura for children, spontaneous remission should be considered.
4) In present plasma fractionation process, it is difficult to inactivate or remove human parvovirus B19 and etc. completely. Accordingly, possibilities of infection cannot be disregarded, and special caution should be taken for catamnesis.
5) Even though a safety plan for the prevention of the spread of infection is prepared, the risk of infection cannot be entirely disregarded since I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection originates from human blood. This risk should be explained to patients.
6) Since I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection 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.
7) Additional administration to patients with Kawasaki Disease should be conducted when additional administration is clearly necessary such as the effectiveness of I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection is insufficient for symptomatic remission (e.g. continuation of fever). (Safety and efficacy for additional administration has not been established)
8) In the case of combined therapy with antibiotics in severe infections, I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection should be used for patients who show insufficient response to proper antimicrobial chemotherapy.
9) There have been published reports that immunoglobulin intravenous injection is related to renal dysfunction, renal failure, osmotic nephrosis, death and etc.
10) 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. Signs or symptoms of thrombosis may include pain and/or swelling of arms or legs with warmth over the affected area, discoloration of arms or legs, unexplained shortness of breath, chest pain or discomfort that worsens on deep breathing, unexplained rapid pulse, chest pain and numbness or weakness on one side of the body.
11) Healthcare professionals should be aware of the risk of 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.

4.5 Interaction with other medicinal products and other forms of interaction

There is a possibility that live vaccines (measles, mumps, rubella and varicella vaccine etc.) do not work for the patients who are treated with I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection.
Therefore, vaccination should be delayed for more than 3 months after administration. If I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection is administered within 14 days after vaccination, re-vaccination should be taken after more than 3 months post I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection administration. After a large bolus administration (more than 200 mg/kg) for the ITP and Kawasaki Syndrome use of live vaccines should be delayed by more than 6 months (In case of low risk of measles infection, measles vaccination should be delayed by more than 11 months).

4.6 Pregnancy and lactation

Safety for pregnant women has not been established. The possibility of parvovirus B-19 infection cannot be excluded from the administration of I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection. In case of parvovirus B-19 infection, fetal disturbances (abortion, hydrops fetalis, fetal death) may occur. I.V.-Globulin SN-JAKEL 50mg/ml Solution for Injection should be given to a pregnant woman only if the expected benefit justifies the possible risk.

4.7 Pediatric use

Safety for low birth weight infants and neonates has not been established.
Aseptic meningitis has been reported following large volume administration of immunoglobulin products for pediatric subject with Idiopathic Thrombocytopenic Purpura and etc.

4.8 Geriatric Use

1) Since elderly patients generally have low physiological function, I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection should be administered with special care.
2) Elderly patients with cerebrovascular and cardiovascular disorders or case history thereof: thromboembolism may occur I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection should be administered with special care.

4.9 Influences to clinical examination results

I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection 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.

4.10 Effects on ability to drive and use machines

Some of the effects mentioned in the Undesirable effects may affect the ability to drive and use machines.

4.11 Undesirable effects

1) Shock
Symptoms of shock may occur occasionally. If dyspnea, wheeze, chest discomfort, drop in blood pressure or weak pulse is watched, administration should be discontinued, and 0.1 – 0.5 mL epinephrine (1:1,000) or the administration of cortisone should be considered.
2) Circulatory
Rapid infusion may result in a drop in blood pressure. (Caution should be taken on patients with A-/Hypogammaglobulinemia).
3) Liver
Jaundice or hepatic impairment with markedly elevated ALT/AST may occur. The patient should be carefully monitored. If there are abnormal findings, proper treatment should be taken.
4) Kidney
Acute renal failure has been reported with the use of immunoglobulin products. The patient should be sufficiently hydrated before dosing and should be thoroughly monitored for decreased urine output, increased creatinine, and increased BUN. If any of these occur, the therapy should be stopped and appropriate treatment should be provided. The administration dosage and rate should be lowered (as low as possible) for patients at high risk for acute renal failure.

5) Central Nervous System
Aseptic meningitis (headache, nuchal rigidity, drowsiness, fever, photophobia, painful eye movements, nausea and vomiting) may occur due to a high dose administration, in which case, the therapy should be stopped and appropriate treatment should be taken.
6) Blood
Because a decrease in platelets may occur with the administration of I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection, patients should be monitored. If this symptom occurs, proper treatment should be taken.

7) Other possible undesirable effects
Drowsiness, chill, chest pain, back pain, gluteal pain and anxiety and etc.
8) Results of post-marketing surveillance in Korea
In accordance to the results of post-marketing surveillance conducted in Korea on 615 patients for 4 years, the incidence rate of adverse events was 17.72% (109/615 patients, total 225 cases) regardless of causal relationship. Among these, serious adverse drug reactions and unexpected adverse drug reactions for which causality cannot be excluded are listed in the table below according to their frequency of occurrence.

		Severe adverse drug reactions 0.33% (2/615 patients, 2 cases)	Unexpected adverse drug reactions 1.46% (9/615 patients 10cases)
Sometimes (0.1% ~ 5%)	General disorders and administration site conditions	pyrexia	-
	Infections and Infestations	-	herpes zoster
	Metabolism and nutrition disorders	-	hypophosphatemia
	Skin and subcutaneous tissue disorders	-	urticaria, pruritus
	Investigations	-	weight increased, blood pressure increased
	Vascular disorders	-	hypertension, cyanosis
	Nervous system disorders	-	dizziness

As a result of the analysis and evaluation of signals based on the reported data of adverse events during post-marketing use (1989 – Sep. 30, 2021) including adverse events of post-marketing surveillance the following adverse events have been identified. However, this does not mean that a causal relationship has been established between the ingredient and the following adverse events.

- Occurs during or immediately after infusion: pyrexia, tachycardia, and blood pressure increased

4.12 Overdose
Overdose may lead to fluid overload and hyperviscosity, particularly in patients at risk, including elderly patients or patients with renal impairment.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: immune sera and immunoglobulins: immunoglobulins, normal human, for intravascular administration, ATC code: J06BA02

Human normal immunoglobulin contains mainly immunoglobulin G (IgG) with a broad spectrum of antibodies against infectious microorganisms.

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 IgG subclasses closely proportional to that in native human plasma. Adequate doses of this medicinal product may restore abnormally low IgG 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 extra-vascular compartments.

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

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

5.3 Preclinical safety data

The IgG in I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection provides antibody activities against a broad spectrum of infectious microorganisms. The three efficacy studies of I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection were evaluated in a primary humoral immunodeficiency (PHID) model using Streptococcus pneumoniae (S. pneumoniae) and Klebsiella pneumoniae (K. pneumoniae) and antibody-induced idiopathic thrombocytopenic purpura (ITP) model. The results were showed equal antibacterial effect and thrombocytopenia-amelioratory effect compared to marketed product.

I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection tested in three safety pharmacology studies. In a cardiovascular study in rats, I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection did not affect the blood pressure and heart rate following a single intravenous administration at a dose of up to 2,000 mg/kg. The results of a central nervous study in ICR mice showed no related effects on body temperature and general behavior following a single dose administration of up to 2,000 mg/kg. In the third study, which measured respiration rate, tidal volume and minute volume, there were no significant differences in these parameters in any I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection groups (2,000 mg/kg or less) compared to the negative control group (physiological saline solution).

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Glycine

Water for injection

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf-life

36 months from the date of manufacture.

6.4 Special precautions for storage
Store in a refrigerator (2°C–8°C) or below 25°C in the original unopened container for up to 36 months from the date of manufacture. Do not freeze. Protect from light.

6.5 Nature and contents of container
25 mL of solution in a vial (Type I glass) with a rubber stopper (chlorobutyl rubber) and flip-off cap.

6.6 Precautions for administration

1) Do not mix and administrate with other medicinal products except for 5 % dextrose in water (D5W). (Do not mix with normal saline)
2) Rapid administration may cause hypotension. Intravenous drip infusion is recommendable. If direct intravenous administration is needed, it should be administered very slowly. (Caution should be taken with A-/Hypogammaglobulinemia patients.)
3) Do not use if the solution is turbid, or if it contains visible particulate matter.
4) I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection contains no preservatives. Each vial should be used within 1 hour and single use only due to microbial contamination. Do not reuse or save for future use.
(I.V.-Globulin SN-JAKEL 100mg/ml Solution for Injection is protein-containing solution which is susceptible to microbial contamination)
5) Do not use any solutions that have been frozen.
6) Visible particle may be generated when the solution collected with siliconized syringes. Inspect visually for particulate matter before use. Do not use if it contains visible particulate matter.

6.7 Precautions for handling
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. MANUFACTURER
GC Biopharma Corp.
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8. PRODUCT REGISTRATION HOLDER
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9. DATE OF REVISION OF THE TEXT
June 2026