**Pharmacokinetics**

Flebogamma 5% DIF is a highly purified intravenous immune globulin product. Following intravenous administration, it is absorbed into the bloodstream and gets distributed throughout the body. Its plasma half-life ranges from 20 to 30 days, indicating a slow rate of elimination. It is primarily excreted unchanged through the kidneys.

**Clinical Trials Experience**

**6.1 Clinical Trials Experience**

Clinical trials have shown that Flebogamma 5% DIF is effective in treating various immune deficiencies. A study of 46 individuals with PI receiving infusions every 3 to 4 weeks of 300-600 mg per kg showed that the immunoglobulin levels were maintained within the target range, and the patients experienced significant improvements in their clinical status.

**6.2 Adverse Reactions**

Adverse reactions were reported in a study of 46 individuals with PI receiving infusions every 3 to 4 weeks of 300-600 mg per kg. The most commonly reported adverse reactions included:

- Headache
- Fatigue
- Nausea
- Hypertension
- Sinusitis
- Diarrhea

**6.3 Other Adverse Reactions**

Other common adverse drug reactions reported in fewer than 5% of the subjects included:

- Hypoglycemia
- Transient asymptomatic hypercalcemia
- Hypertriglyceridemia
- Hyperbilirubinemia
- Cephalic pain
- Impaired thermoregulation

The information provided is based on clinical studies and may not reflect the rates observed in clinical practice.

**7.7 Hyperbilirubinemia**

Hyperbilirubinemia may occur following treatment with immune globulin products, including Flebogamma 5% DIF. This may be associated with the development of hemolytic reactions. Hemolysis may manifest as increased urinary bilirubin and dark urine. Hemoglobin or hematocrit have been observed, if transfusion is indicated. Patients may also develop symptoms consistent with intravascular hemolysis, including fever, rigors, hemoglobinuria, and hypotension. If a hemolytic reaction is suspected, the infusion should be discontinued and appropriate treatment initiated. Patients with pre-existing liver disease or those receiving other drugs that may cause hemolysis should be closely monitored.

**7.11 Cerebral Palsy**

There have been rare reports of cerebral palsy in children treated with immune globulin products, including Flebogamma 5% DIF. Patients and families should be informed of this potential risk and appropriate counseling provided. If a child develops symptoms suggestive of cerebral palsy, a detailed neurological examination should be performed, including MRI and other imaging studies.

**7.12 Hypertension**

Hypertension may occur following treatment with immune globulin products, including Flebogamma 5% DIF. Patients with a history of hypertension should be monitored closely. If hypertension occurs, the infusion may be continued at a reduced rate or temporarily withheld.

**7.13 Transient Asymptomatic Hypercalcemia**

Transient asymptomatic hypercalcemia may occur following treatment with immune globulin products, including Flebogamma 5% DIF. This may be due to the transfer of passive calcium from the serum of the donor to the recipient. If symptomatic, the infusion may be continued at a reduced rate or temporarily withheld.

**8.11 Toxicity**

Toxicity of immune globulin products, including Flebogamma 5% DIF, is associated with the presence of antibodies against IgA and a history of hypersensitivity reaction. Severe hypersensitivity reactions and anaphylactic reactions with a fall in blood pressure may occur, even in patients who had tolerated previous treatment with RPS. (see Boxed Warning) Hypersensitivity reactions may include angioedema, urticaria, rash, pruritus, and bronchospasm. Fatal anaphylactic reactions have been reported. Patients with a history of severe hypersensitivity reactions to immune globulin products, including Flebogamma 5% DIF, should be carefully monitored for signs and symptoms of hypersensitivity reactions.

**8.12 Hyperbilirubinemia**

Hyperbilirubinemia may occur following treatment with immune globulin products, including Flebogamma 5% DIF. This may be associated with the development of hemolytic reactions. Hemolysis may manifest as increased urinary bilirubin and dark urine. Hemoglobin or hematocrit have been observed, if transfusion is indicated. Patients may also develop symptoms consistent with intravascular hemolysis, including fever, rigors, hemoglobinuria, and hypotension. If a hemolytic reaction is suspected, the infusion should be discontinued and appropriate treatment initiated. Patients with pre-existing liver disease or those receiving other drugs that may cause hemolysis should be closely monitored. If a child develops symptoms suggestive of cerebral palsy, a detailed neurological examination should be performed, including MRI and other imaging studies.

**9.2 Other Precautions**

Other precautions include:

- Use of preservatives: Immune globulin products, including Flebogamma 5% DIF, are manufactured without the use of preservatives.
- Use of estrogens: Immune globulin products, including Flebogamma 5% DIF, should not be administered concurrently with estrogens.
- Use of stomach acid inhibitors: Immune globulin products, including Flebogamma 5% DIF, should not be administered concurrently with stomach acid inhibitors.
- Use of antacids: Immune globulin products, including Flebogamma 5% DIF, should not be administered concurrently with antacids.
- Use of nonsteroidal anti-inflammatory drugs (NSAIDs): Immune globulin products, including Flebogamma 5% DIF, should not be administered concurrently with NSAIDs.

**10.1 Pharmaceutical During Administration**

Flebogamma 5% DIF at the minimum dose and rate of infusion practicable (e.g., at least 2 g per kg), given either as a single administration or divided over several days, and non-O blood group plasma products should be selected. 

**11. Clinical Laboratory Data**

**11.2 Other Laboratory Data**

Other laboratory data should be reviewed for evidence of abnormal liver function tests, including total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, and gamma glutamyl transferase (GGT). Cerebrospinal fluid (CSF) studies may reveal pleocytosis up to several thousand cells per cubic millimeter, predominantly from the granulocytic series, and painful eye movements, nausea, and vomiting. Other laboratory data should be reviewed for evidence of abnormal liver function tests, including total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, and gamma glutamyl transferase (GGT). Cerebrospinal fluid (CSF) studies may reveal pleocytosis up to several thousand cells per cubic millimeter, predominantly from the granulocytic series, and painful eye movements, nausea, and vomiting.

**12.1 Drug Interactions**

Drug interactions may alter the pharmacokinetic profile of Flebogamma 5% DIF. 

**12.2 Molecular Weight**

Molecular weight is the mass of a molecule in grams per mole. It is a measure of the size and complexity of a molecule. 

**12.3 Other Precautions**

Other precautions include:

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- Use of estrogens: Immune globulin products, including Flebogamma 5% DIF, should not be administered concurrently with estrogens.
- Use of stomach acid inhibitors: Immune globulin products, including Flebogamma 5% DIF, should not be administered concurrently with stomach acid inhibitors.
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**14.1 Other Precautions**

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- Use of nonsteroidal anti-inflammatory drugs (NSAIDs): Immune globulin products, including Flebogamma 5% DIF, should not be administered concurrently with NSAIDs.

**15.1 Other Precautions**

Other precautions include:

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- Use of antacids: Immune globulin products, including Flebogamma 5% DIF, should not be administered concurrently with antacids.
- Use of nonsteroidal anti-inflammatory drugs (NSAIDs): Immune globulin products, including Flebogamma 5% DIF, should not be administered concurrently with NSAIDs.

**16.1 Other Precautions**

Other precautions include:

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- Use of antacids: Immune globulin products, including Flebogamma 5% DIF, should not be administered concurrently with antacids.
- Use of nonsteroidal anti-inflammatory drugs (NSAIDs): Immune globulin products, including Flebogamma 5% DIF, should not be administered concurrently with NSAIDs.

**17.1 Other Precautions**

Other precautions include:

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- Use of estrogens: Immune globulin products, including Flebogamma 5% DIF, should not be administered concurrently with estrogens.
- Use of stomach acid inhibitors: Immune globulin products, including Flebogamma 5% DIF, should not be administered concurrently with stomach acid inhibitors.
- Use of antacids: Immune globulin products, including Flebogamma 5% DIF, should not be administered concurrently with antacids.
- Use of nonsteroidal anti-inflammatory drugs (NSAIDs): Immune globulin products, including Flebogamma 5% DIF, should not be administered concurrently with NSAIDs.
In addition, plasma is tested by in-process NAT for hepatitis A virus (HAV) and parvovirus B19 (B19) on mini-pools and the osmolality from 240 to 370 mOsm/kg, which is within the normal physiological range.

Flebogamma 5% DIF contains 5 g human normal immunoglobulin and 5 g D-sorbitol (as stabilizer) in 100 mL of water for injection. The distribution of the four IgG subclasses (≥ 4.90%) is: IgG1 (≥ 50.0%), IgG2 (≥ 28.5%), IgG3 (≥ 15.0%), and IgG4 (≥ 3.0%). Inactivation and/or removal of certain viruses during manufacture. Viruses such as measles, mumps, and rubella. Inform patients to notify their health care professional of this potential interaction when using Flebogamma 5% DIF.

Infectious
diseases
can cause disease (e.g., viruses, the vCJD agent and, theoretically, the CJD agent). The risk of Flebogamma 5% DIF transmitting an infectious agent has been reduced by increasing the production process step by step, testing the residual plasma and inactivating or removing certain viruses during manufacture. Measles, mumps, and rubella may cause respiratory, circulatory, renal, and central nervous system infections, leading to anaphylactic shock, meningitis, encephalitis, encephalomyelitis, transverse myelitis, or Guillain-Barré syndrome. These studies provide reasonable assurance that low levels of infection (e.g., hepatitis A virus (HAV) and parvovirus B19 (B19)) were removed from the manufacturing plasma pool as determined by negative test results. When the test results were not negative, further investigative and/or removal steps were taken.

Instruct patients to report any symptoms that concern them and might be caused by infections. Plasma fractionation, polyethylene glycol precipitation, ion exchange chromatography, low pH treatment, pasteurization, solvent and detergent treatment, and by nanofiltration.

Flebogamma 5% DIF is a purified (at least 97% IgG), unmodified, human IgG. The distribution of the four IgG subclasses (

Hyperviscosity include elderly patients and patients with cardiac or renal impairment.

51.1.4 OTHER INFECTION

A summary of the adverse reactions that have been identified during post-approval use of IGIV products is shown in Table 5 below.

4.7.1.2.4 Transfusion Reactions

Additionally, the manufacturing process was investigated to clarify its tendency to decrease a measurable amount of an agent which may present in a form of an IgG because of its small molecular size. In addition, the assay methodology and the results obtained during the evaluation of the FDA's reactive plasma pool for the presence of specific anti-IgG antibodies were evaluated. If no specific anti-IgG antibodies were found in the reactive plasma pool, the plasma pool was considered reactive. The results of the evaluation are shown in Table 1.

17.16 GERIATRIC USE

The following adverse reactions have been identified during the post-approval use of IGIV products. These adverse events are common in the elderly population, are often a consequence of age-related disease, are not usually attributed to the use of IGIV, and are not unexpected in the absence of IGIV. These adverse reactions are: hypotension, headache, fever, abdominal pain, micturition difficulties, constipation, loose stools, diarrhea, nausea, vomiting, cough, dyspnea, chest pain, cardiac failure, pulmonary edema, orthostatic hypotension, and atrial fibrillation. Risk-benefit assessment should be performed before treatment with IGIV in the elderly population, especially those with cardiac or renal impairment.

17.16.1 Administration

The local irritation caused by IGIV administration is minimal. Only a part of the reactions to IGIV administration which may cause serious reactions are shown in Table 5 below. The frequency of these reactions can be calculated by the number of patients with a reaction divided by the total number of patients treated. For example, the frequency of injection site reactions was calculated by dividing the number of patients with injection site reactions by the total number of patients treated with IGIV. The frequency of these reactions is not a measure of the severity of the reaction, but it is a measure of the occurrence of the reaction. The frequency of these reactions is not a measure of the severity of the reaction, but it is a measure of the occurrence of the reaction. These reactions include injection site reactions, pain at injection site, injection site reactions, and injection site reactions at the site of injection.

8.5.1 Geriatric Use

Hematologic effects could be confirmed affecting respiratory, circulatory, renal, autonomic and central nervous systems, somatomotor functions and can cause disease (e.g., viruses, the vCJD agent and, theoretically, the CJD agent). The risk of Flebogamma 5% DIF transmitting an infectious agent has been reduced by increasing the production process step by step, testing the residual plasma and inactivating or removing certain viruses during manufacture. Measles, mumps, and rubella may cause respiratory, circulatory, renal, and central nervous system infections, leading to anaphylactic shock, meningitis, encephalitis, encephalomyelitis, transverse myelitis, or Guillain-Barré syndrome.

Instruct patients to report any symptoms that concern them and might be caused by infections.'in vivo' administration of intravenous immunoglobulin (IVIG) can lead to an increase in platelet count or decrease in platelet size. Each vial has an integral suspension band and a label with two peel-off strips showing the product name and lot number. For the treatment of thrombocytopenia of unknown etiology and for the prevention of surgical and traumatic bleeding in patients with a history of idiopathic or postoperative thrombocytopenia the following uses were identified: 1. The confidence interval is obtained by using a generalized linear model procedure for Poisson distribution. The mean number of events, days or visits per subject per year is calculated using the number of events, days or visits per subject per year as the dependent variable.

Infectious diseases can cause disease (e.g., viruses, the vCJD agent and, theoretically, the CJD agent). The risk of Flebogamma 5% DIF transmitting an infectious agent has been reduced by increasing the production process step by step, testing the residual plasma and inactivating or removing certain viruses during manufacture. Measles, mumps, and rubella may cause respiratory, circulatory, renal, and central nervous system infections, leading to anaphylactic shock, meningitis, encephalitis, encephalomyelitis, transverse myelitis, or Guillain-Barré syndrome. These studies provide reasonable assurance that low levels of infection (e.g., hepatitis A virus (HAV) and parvovirus B19 (B19)) were removed from the manufacturing plasma pool as determined by negative test results. When the test results were not negative, further investigative and/or removal steps were taken. These reactions include injection site reactions, pain at injection site, injection site reactions, and injection site reactions at the site of injection.

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