Be DIFferent

- Demonstrated **tolerability and proven efficacy** in both immune replacement and autoimmune disease.\(^1,2\)

- **Each patient is different**: Flebogamma\(^\text{®}\) DIF is available in 50mg/mL and 100mg/mL concentrations, allowing you to choose the best product to meet each patient’s individual needs.

- **An outstanding safety record over 20 years**, with almost 100 million grams of Flebogamma\(^\text{®}\)/Flebogamma\(^\text{®}\) DIF administered to patients worldwide.\(^3\)

**GRIFOLS**
Flebogamma® DIF
Human Normal Immunoglobulin (IVig)

50 mg/ml  100 mg/ml

Distributed in Ireland by:
Caragen Ltd
No. 7 Regus, The Gables,
Torquay Road, Foxrock,
Dublin D18 A2N7, IRELAND

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Email: info@caragen.com
Web: www.caragen.com
**ABREVIATED PRESCRIBING INFORMATION**

Flebogamma® DIF 50mg/mL, & 100mg/mL solution for infusion

**Abbreviated Prescribing Information**

Flebogamma® DIF 50mg/mL, & 100mg/mL solution for infusion

Please refer to Summary of Product Characteristics (SmPC) before prescribing.

**Therapeutic indications:** Flebogamma® DIF is indicated for: Replacement therapy in adults, children & adolescents (2-18 years) in: Primary immunodeficiency syndromes with impaired production; hypogammaglobulinemia & recurrent bacterial infections in patients with chronic lymphocytic leukaemia, in whom prophylactic antibiotics have failed; hypogammaglobulinemia & recurrent bacterial infections in plateau-phase multiple myeloma patients who failed to respond to pneumococcal immunisation; hypogammaglobulinemia in patients after allogeneic haematopoietic stem cell transplantation (HSCT); congenital AIDS with recurrent bacterial infections. Immunomodulation in adults, children & adolescents (2-18 years) in: Primary immune thrombocytopenia (ITP), in patients at high risk of bleeding or prior to surgery to correct the platelet count; Guillain Barré Syndrome; Kawasaki disease.

**Presentation:** The solution is clear, or slightly opalescent and is colourless, or pale yellow. Flebogamma® DIF is isotonic, with an osmolality from 240 to 370 mOsm/kg. Flebogamma® DIF is supplied in 50ml, 100ml, 200ml solution in a vial (type II glass) with stopper (chloro-butyl rubber). Not all pack sizes may be marketed.

**Dosage:** In replacement therapy the dose may need to be individualised for each patient dependent on the pharmacokinetic and clinical response. The following dose regimens are given as a guideline. Replacement therapy in primary immunodeficiency syndromes: The dose should achieve a trough level of IgG (measured before the next infusion) of at least 5 - 6g/L. Three to six months are required after the initiation of therapy for equilibration to occur. The recommended starting dose is 0.4 - 0.8g/kg followed by at least 0.2g/kg/month every three to four weeks. The dose interval when steady state has been reached varies from 3 – 4 weeks. Trough levels should be measured and assessed in conjunction with the incidence of infection. To reduce the rate of infection, it may be necessary to increase the dosage and aim for higher trough levels. Hypogammaglobulinemia and recurrent bacterial infections in patients with chronic lymphocytic leukaemia: the recommended dose is 0.2 - 0.4g/kg every three to four weeks. Hypogammaglobulinemia in patients after allogeneic haematopoietic stem cell transplantation: The recommended dose is 0.2 - 0.4g/kg every three to four weeks. Hypogammaglobulinemia in patients with congenital AIDS: The treatment can be repeated if relapse occurs. Guillain Barré Syndrome: 0.4g/kg/day for 5 days. Kawasaki disease: 1.6g/kg for 5 days.

**Contra-Indications:** The product is contraindicated in children aged under 0-2 years (see Special warnings & Precautions). Hypersensitivity to any of the components. Hypersensitivity to human immunoglobulins, especially when the patient has antibodies against IgA. Fructose intolerance.

**Special warnings and Precautions:** Each ml of this medicinal product contains 50 mg of sorbitol. Patients with rare hereditary problems of fructose intolerance must not take this medicine. In persons more than 2 years old with HFI, a spontaneous aversion for fructose-containing foods develops and may be combined with the onset of symptoms (vomiting, gastro-intestinal disorders, apathy, height and weight retardation). Therefore a detailed history with regard to HFI symptoms has to be taken of each patient prior to receiving Flebogamma® DIF. In case of inadvertent application and suspicion of hereditary fructose intolerance the infusion has to be stopped immediately, normal glycaemia has to be re-established and organ function has to be stabilized by means of intensive care. Interferences with determination of blood glucose levels are not expected. Certain severe adverse drug reactions may be related to the rate of infusion. The recommended infusion rate given in the SmPC must be closely followed. Patients must be closely monitored and carefully observed for any symptoms throughout the infusion period. It is recommended to monitor vital signs when administering Flebogamma DIF to paediatric patients. Certain adverse reactions may occur more frequently: In case of high rate of infusion, in patients with hypo- or agammaglobulinemia with or without IgA deficiency, in patients who receive human normal immunoglobulin for the first time, or in rare cases, when the human normal immunoglobulin product is switched or when there has been a long interval since the previous infusion. Caution should be exercised in prescribing and infusing IgV in obese patients and in patients with pre-existing risk factors for thrombotic events (see SmPC for further details).

**Undesirable Effects:** The most reported post-marketing ADRs received since the product was authorised for both concentrations were chest pain, flushing, blood pressure increased and decreased, malaise, dyspnoea, nausea, vomiting, pyrexia, back pain, headache and chills. Rarely human normal immunoglobulins may cause a sudden fall in blood pressure and, in isolated cases, anaphylactic shock, even when the patient has shown no hypersensitivity to previous administration. Cases of reversible aseptic meningitis syndrome, isolated cases of reversible haemolytic anaemia/haemolysis and rare cases of transient cutaneous ulcerations, have been observed with human normal immunoglobulin. Increase in serum creatinine level and/or acute renal failure have been observed. Very rarely: Thromboembolic reactions such as myocardial infarction, stroke, pulmonary embolism, deep vein thromboses. For further information including safety regarding transmissible agents see the SmPC. Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the HPRA Pharmacovigilance.

**Incompatibilities:** This medicinal product must not be mixed with other medicinal products or intravenous fluids. It should be administered by a separate intravenous line.

**Marketing Authorisation Number:** EU/1/07/404/001-005 50mg/mL; & EU/1/07/404/006-008 100mg/mL Marketing Authorisation Holder: Instituto Grifols S.A, Can Guasc 2, Pareds del Vallès, 08150 Barcelona, Spain. API last revised: June 2016

**Ref:** FAX 16/01/SmPC-APIR2016

Information about adverse event reporting can be found at www.hpra.ie. You can report side effects directly via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 667 4971; Fax: +353 1 667 2517 or E-mail: medsafety@hpra.ie or medical@athlone-laboratories.com

For a full copy of the SPC or additional information please contact Caragen: Caragen Ltd. No. 7 Regus, The Gables, Torquay Road, Foxrock, Dublin D18 A2N7, IRELAND Tel: +353 1 566 2609 Fax:+353 1 688 4969 Email: info@caragen.com Web: www.caragen.com
Each patient is different: Flebogamma® DIF is available in 5% and 10% concentrations, allowing you to choose the best product to meet each patient’s individual needs.

**High purity, functional integrity, and osmolality** within the physiological range

▶ Osmolality, sodium, sugar and IgA content can affect the clinical tolerability in your patients. Choose the right product based on your patients’ needs:

▶ Hyperosmolar solutions, administered intravenously may cause fluid shifts leading to haemodynamic changes, thromboembolic incidents, or renal complications

▶ Low sodium preparations may make Flebogamma® DIF appropriate for patients with restricted sodium intake; higher incidences of adverse events and thromboembolic complications may be seen with increased salt concentrations

▶ Sugar content has been associated with adverse events, especially renal failure or insufficiency; up to 90% of the IVIG-associated renal adverse events have been linked to sucrose-containing preparations

▶ Patients with selective IgA deficiency and the ability to produce antibodies may be at risk for developing IgE- or IgG-type anti-IgA antibodies

**Risk factors considerations**

<table>
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<th>Patient risk factors</th>
<th>Sugar content</th>
<th>Sodium content</th>
<th>Osmolality</th>
<th>Volume load</th>
<th>IgA</th>
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<td>(Pre) Diabetes</td>
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3 Data on file. Instituto Grifols, S.A.
4 Flebogamma® DIF Summary of product characteristics.
Each patient is different: Flebogamma® DIF is available in 5% and 10% concentrations, allowing you to choose the best product to meet each patient’s individual needs.

Sucrose-free, very low levels of IgA and sodium, and no preservatives

- Flebogamma® DIF is a highly purified IVIG with high functional integrity of the IgG molecule suitable for your patients as:
  - It is preservative-free
  - Its osmolality is within the physiological range (240-350 mOsm/kg)
  - It contains trace amounts of sodium (<3.2 mmol/L)
  - It uses sorbitol as stabilizer (no sucrose, no maltose and no glucose), a polyol that plays a physiologically protective role as an organic osmolyte in the kidneys, which translates into a lower risk of acute renal failure
  - It contains trace amounts of IgA (<0.003 mg/mL), being one of the lowest concentrations of IgA in the IVIG market

A more careful matching of patient risk factors with the attributes or deficiencies of a given product becomes important.

Flebogamma® DIF is a highly purified IVIG with trace amounts of IgA and sodium and stabilized with sorbitol, making it suitable for patients with certain risk factors

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11 Gürkan H.M et al. Information for healthcare providers on general features of IVIG with emphasis on differences between commercially available products. Autoimmunity reviews 2010;9(8):553-559

*Mean values: Flebogamma® 5% DIF (50 mg/mL), n=156. Flebogamma® 10% DIF (100 mg/mL), n=85.
Each patient is different: Flebogamma® DIF is available in 5% and 10% concentrations, allowing you to choose the best product to meet each patient’s individual needs.

Flebogamma® DIF is convenient for:

✶ Your patients:

◆ Patient risk factors and certain clinical conditions should be considered when selecting which concentration of IVIG to use.

5% concentration

• It may be an appropriate choice for patients who have certain frequent adverse reactions to infusions of IVIG.
• It may be suitable also for patients who would benefit from additional fluid.

10% concentration

• It can be infused in a lower volume being able to meet the needs of patients at risk of volume overload, including patients with heart failure or renal dysfunction.

✶ Your clinical practice:

◆ Ready-to-use liquid
◆ Storable at room temperature for the entire two-year shelf life* (Can also be stored at 2-8°C with no change in stability)