## ABBREVIATED PRESCRIBING INFORMATION

### Flebogamma® DIF 50mg/mL solution for infusion

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

**Therapeutic indications:** Flebogamma® DIF 50mg/ml is indicated for: Replacement therapy in adults, children & adolescents (2-18 years) in: Primary immunodeficiency syndromes with impaired antibody production; Secondary immunodeficiencies (SID) in patients who suffer from severe or recurrent infections, ineffective antimicrobial treatment and either proven specific antibody failure (PSAF)* or serum IgG level of <4 g/l. *PSAF= failure to mount at least a 2-fold rise in IgG antibody titre to pneumococcal polysaccharide and polypeptide antigen vaccines 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 (in conjunction with acetylsalicylic acid; see 4.2 of SmPC); Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP); Multifocal motor neuropathy (MMN).

**Presentation:** The solution is clear, or slightly opalescent and is colourless, or pale yellow. Flebogamma® DIF 50mg/ml is isotonic, with an osmolality from 240 to 370 mOsm/kg. Flebogamma® DIF 50mg/ml 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 & Method of administration:** The dose may need to be individualised for each patient dependent on the clinical response. Dose based on body weight may require adjustment in underweight or overweight patients. 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 6g/l or within the normal reference range for the population age. Three to six months are required after the initiation of therapy for equilibration (steady-state IgG levels) 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 required to achieve a trough level of IgG of 6 g/l is of the order of 0.2 - 0.8 g/kg/month. The dose interval when steady state has been reached varies from 3 – 4 weeks. IgG trough levels should be measured and assessed in conjunction with the incidence of infection. To reduce the rate of bacterial infection, it may be necessary to increase the dosage and aim for higher trough levels. *Secondary immunodeficiencies:* The recommended dose is 0.2 - 0.4g/kg every three to four weeks. IgG trough levels should be measured and assessed in conjunction with the incidence of infection. Dose should be adjusted as necessary to achieve optimal protection against infections, an increase may be necessary in patients with persisting infection; a dose decrease can be considered when the patient remains infection free. *Primary Immune Thrombocytopenia:* For the treatment of an acute episode, 0.8 - 1g/kg on day one, which may be repeated once within 3 days, or 0.4g/kg daily for two to five days. The treatment can be repeated if relapse occurs. *Guillain Barré syndrome:* 0.4g/kg/day for 5 days (possible repeat of dosing in case of relapse). *Kawasaki disease:* 2g/kg should be administered as a single dose. Patients should receive concomitant treatment with acetylsalicylic acid. *Chronic inflammatory demyelinating polyneuropathy (CIDP):* Starting dose: 2 g/kg divided over 2 - 5 consecutive days. Maintenance doses: 1 g/kg over 1 - 2 consecutive days every 3 weeks.

*Multifocal motor neuropathy (MMN):* Starting dose: 2 g/kg divided over 2 - 5 consecutive days. Maintenance dose: 1 g/kg every 2 to 4 weeks or 2 g/kg every 4 to 8 weeks. For further information on the indications and dosing, please refer to the SmPC.

Flebogamma DIF 50mg/ml should be infused intravenously at an initial rate of 0.01 - 0.02ml/kg/min for the first thirty minutes In case of adverse reaction, either the rate of administration must be reduced or the infusion stopped. If well tolerated, the rate of administration may gradually be increased to a maximum of 0.1ml/kg/min.

**Contra-Indications (see also SmPC):** The product is contraindicated in children aged 0-2 years (see Special warnings & Precautions). Hypersensitivity to the active substance (human immunoglobulins) or to any of the excipients listed in the SmPC. Hypersensitivity to human immunoglobulins, especially in patients with antibodies against IgA. In babies and young children (aged 0 - 2 years) hereditary fructose intolerance (HFI) may not yet be diagnosed and may be fatal, thus, they must not receive this medicinal product. Patients with selective IgA deficiency who developed antibodies to IgA, as administering an IgA-containing product can result in anaphylaxis.

**Special warnings and Precautions (see also SmPC): 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 50mg/ml. 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.** *Precautions for use:* It is recommended to monitor vital signs when administering Flebogamma® DIF to paediatric patients. Potential complications can often be avoided by ensuring that patients: are not sensitive to human normal immunoglobulin by initially injecting the product slowly (at an initial rate of 0.01- 0.02 ml/kg/min); are carefully monitored for any symptoms throughout the infusion period. In particular, patients naive to human normal immunoglobulin, patients switched from an alternative IVIg product or when there has been a long interval since the previous infusion should be monitored at the hospital during the first infusion and for the first hour after the first infusion, in order to detect potential adverse signs. All other patients should be observed for at least 20 minutes after administration. IVIG administration requires adequate hydration prior to infusion, monitoring of urine output and serum creatinine levels and avoidance of concomitant use of loop diuretics. Certain adverse reactions (e.g. headache, flushing, chills, myalgia, wheezing, tachycardia, lower back pain, nausea, and hypotension) may be related to the rate of infusion. Hypersensitivity reactions are rare. Caution should be exercised in prescribing and infusing IVIg in obese patients and in patients with pre-existing risk factors for thrombotic events. (see SmPC for further details).Cases of acute renal failure have been reported in patients receiving IVIg therapy. Aseptic meningitis syndrome has been reported to occur in association with IVIg treatment. Haemolytic anaemia can develop subsequent to IVIg therapy due to enhanced red blood cells (RBC) sequestration. IVIg recipients should be monitored for clinical signs and symptoms of haemolysis. A transient decrease in neutrophil count and/or episodes of neutropenia, sometimes severe, have been reported after treatment with IVIgs. This typically occurs within hours or days after IVIg administration and resolves spontaneously within 7 to 14 days. In patients receiving IVIg, there have been some reports of acute non-cardiogenic pulmonary oedema [Transfusion Related Acute Lung Injury (TRALI)]. . Immunoglobulin administration may impair the efficacy of live attenuated virus vaccines and may result in transient misleading positive results in serological testing. Use with caution in pregnant women and breast-feeding mothers. When medicinal products prepared from human blood or plasma are administered, the possibility of transmitting infective agents cannot be totally excluded. Overdose may lead to fluid overload and hyperviscosity, particularly in patients at risk, including elderly patients or patients with cardiac or renal impairment. Information on overdose in children has not been established with Flebogamma® DIF 50mg/ml. However, as in adult population, overdose may lead to fluid overload and hyperviscosity as with any other intravenous immunoglobulins.

**Undesirable Effects (see also SmPC):** Adverse reactions such as caused by human normal immunoglobulins encompass : chills, headache, abdominal pain, pain, rigors, injection site pain, bronchitis, wheezing, diarrhoea, urticaria, tachycardia, Diastolic hypo- and hypertension, Coombs test positive, Myalgia, pyrexia, pain. Blood pressure systolic increased, Body temperature increased, dizziness, vomiting, allergic reactions, nausea, arthralgia, low blood pressure and moderate low back pain (common); rarely human normal immunoglobulins may cause reversible haemolytic reactions; especially in those patients with blood groups A, B, and AB and (rarely) haemolytic anaemia requiring transfusion; (rarely) 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 and rare cases of (rarely) transient cutaneous reactions (including cutaneous lupus erythematosus - frequency unknown) have been observed with human normal immunoglobulin. Reversible haemolytic reactions have been observed in patients, especially those with blood groups A, B, and AB; rarely, haemolytic anaemia requiring transfusion may develop after high dose IVIg treatment; 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; cases of Transfusion Related Acute Lung Injury (TRALI). For safety information with respect to transmissible agents, see 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 UK Yellowcard Scheme.

**Incompatibilities:** In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products, nor with any other IVIg products.

**Pharmaceutical Precautions:** Flebogamma® DIF 50mg/ml should not be stored above 30ºC. The contents must not be frozen. Flebogamma® DIF 50mg/ml may be stored for 2 years under these conditions. The product should be brought to room or body temperature before use. The solution should be clear or slightly opalescent. Do not use solutions that are cloudy or have

deposits. Any unused product or waste material should be disposed of in accordance with local requirements.

**Basic NHS Price:** £60 per gram

**Legal Category:** POM

**Marketing Authorisation Number:** EU/1/07/404/001-005 / PLGB 12930/0019

**Marketing Authorisation Holder:** Instituto Grifols S.A, Can Guasc 2, Parets del Vallès, 08150 Barcelona, Spain.

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard
Adverse events should also be reported to Grifols UK Ltd. Please contact Medical Information Services on 0845 241 3090 or email medinfo.uk@grifols.com