警　語

● 孕婦及授乳

尚未有完整臨床試驗來證實本品用於孕婦之安全性。故此對於孕婦或母奶餵養期之婦女，有明確指示時才給藥。免疫球蛋白長期臨床試驗表示對懷孕過程、胎兒或新生兒不會有危害性之影響。

● 對駕駛能力之影響

不適用

劑　量

使用劑量及方法視適應症而定。

替代治療之劑量依每位患者的藥品動力學及臨床反應而定，下列為用法之準則:

原發性免疫缺乏症候群之替代治療

在計量方法中IgG至少應達到谷底值4-6g/L (下次給藥前測得)。初次治療後需間隔3-6個月使之平衡，建議起始劑量為0.4-0.8g/kg，接著每3週至少投予0.2g/kg。

為使達到谷底值6g/L，每月需投予劑量0.2-0.8g/kg，達到穩定狀態之投藥間隔為2-4週。應測量谷底值以調整劑量及投藥間隔。

原發性血小板減少紫癜症

急性發作時於治療第一天投予0.8-1g/kg，三天內可重複投予一次，或每天投予0.4g/kg達2-5天。如果復發，可重複治療。

川崎氏症 (Kawasaki disease)

於2-5天分次投予1.6-2.0g/kg或投予單一劑量2.0g/kg。

病人應同時合併乙醯水楊酸治療。

使用建議劑量如下表:

適　應　症	劑　量	投　藥　頻　率
原發性免疫缺乏 症候群之替代治療	初劑量：0.4-0.8g/kg 隨後：0.2-0.8g/kg	每2-4週獲得IgG之谷底值 至少為4-6g/l。
免疫調節作用： 原發性血小板 減少紫癜症	0.8-1g/kg 或 0.4g/kg/天	第一天，3天內可重複投予一次。 2-5天。
川崎氏症 (kawasaki disease)	1.6-2g/kg 或 2g/kg	合併給予乙醯水楊酸，於2-5天內分多次投予。 合併乙醯水楊酸一次投予。

使用 方法

注射前產品加溫至室溫乃至體溫。本品供靜脈注射用，在最初30分鐘內以0.01-0.02ml/kg/分鐘速率注射。若病人可承受則將速率提高至0.04ml/kg/分鐘，並可維持此速率。若出現不良反應，即降低速率或暫停注射直至症狀減退為止。而後，可以病人承受的速率恢復注射。

劑量過多

由於曾未有過量之報告，其後果無法知曉。

不良 反應

臨床研究已確認本品在以建議之速率注射時，病人可承受並不會產生不良反應。但，首次注射，尤其曾未接受過治療的丙球缺少症、過少症之病人或曾經使用過其他品牌之病人，可能導致全身性副作用。有些副作用因被輸注之抗體與病人血中及組織內游離之抗原之間的反應而出現。不良反應可能包括面紅、胸悶、惡寒、發燒、眩暈、噁心、輕徵的背痛以及血壓下降。與其他靜脈注射免疫球蛋白製劑相較，本品大劑量給藥也罕見無菌性胸膜炎及溶血性貧血。若出現本仿單未提及之不良反應，即通知醫師或藥師。

貯　存

本品應存放於30℃以下，勿冷凍。未用完之藥液，因有細菌污染之可能，應予丟棄。請存放於小孩無法看與拿到之處。

有 效 期

本品有效期於標籤上標示，過期不可使用。

包　裝

本品以下列包裝供應：0.5g、2.5g、5g、10g、20g

本藥限由醫師使用

製 造 商：INSTITUTO GRIFOLS, S.A.
地　　址：Poligono Levante c/Can Guasch, 2,
08150 Parets del Valles, Barcelona, SPAIN
藥商名稱：台灣綠十字股份有限公司
地　　址：台北市承德路三段244號6樓

Instituto Grifols, S.A. Can Guasch, 2 - Parets del Vallès 08150 Barcelona - SPAIN

3046364

GRIFOLS

Flebogamma® 5% DIF
0.5 - 2.5 - 5 - 10 - 20 g

HUMAN NORMAL IMMUNOGLOBULIN FOR INTRAVENOUS USE
Solution for infusion
License no. 000672

WARNING: THROMBOSIS
1. Thrombosis may occur with products containing human immunoglobulin.
2. Risk factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling vascular catheters, hyperviscosity, and cardiovascular risk factors.
3. Patients with unknown thrombosis risk factors may develop thrombosis.
4. Patients at risk for thrombosis should receive human immunoglobulin products at the minimum effective dose and slowest infusion rate practicable.
5. Ensure adequate hydration in patients before administration.
6. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity.

Composition

	0.5 g	2.5 g	5 g	10 g	20 g
- Active ingredient:					
Human normal immunoglobulin	0.5 g	2.5 g	5 g	10 g	20 g
- Excipients:					
D-Sorbitol					
Water for injection q.s.	10 ml	50 ml	100 ml	200 ml	400 ml

The percentage of IgG subclasses determined by radial immunodiffusion (The Binding Site), is approx.: 68.7% IgG_1, 25.9% IgG_2, 3.7% IgG_3 and 1.78% IgG_4.
IgA content is lower than 0.05 mg/ml.

Pharmaceutical form and content

Solution for infusion containing 50 g/l human normal immunoglobulin.

Activity

Flebogamma® 5% DIF is a solution for infusion of unmodified immunoglobulins isolated from human plasma.

Therapeutic indications

Flebogamma® 5% DIF is indicated for:
Primary immunodeficiency syndromes:
Immunomodulation
Idiopathic thrombocytopenic purpura (ITP), in children or adults at high risk of bleeding or prior to surgery to correct the platelet count.
Kawasaki disease.

Contraindications

Intolerance to homologous immunoglobulins, specially in very rare cases of IgA deficiency, when the patient has antibodies against IgA.
Allergic response to other components.

Precautions

Thrombosis: Treatment with products containing human immunoglobulin may develop thrombosis. Risk factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling vascular catheters, hyperviscosity, and cardiovascular risk factors. Patients with unknown thrombosis risk factors may develop thrombosis. Patients at risk of hyperviscosity, including cryoglobulins, fasting chylomicronemia / high triglyceride levels or monoclonal gammopathies, should consider baseline assessments of blood viscosity. Patients at risk for thrombosis should receive this product at the minimum effective dose and slowest infusion rate practicable. Ensure adequate hydration in patients before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity.

Patients with agamma- or extreme hypogammaglobulinaemia who have never before received immunoglobulin therapy or whose time from last treatment is greater than 8 weeks, may be at risk of developing inflammatory reactions on infusion of Flebogamma® 5% DIF. Such reactions appear to be related to the rate of infusion. They are manifested by a rise in temperature, chills, nausea and vomiting. Vital signs should be monitored continuously and the patient should be carefully observed throughout the infusion.

The rate of administration specified in “instructions for use” should be closely followed, at least until the physician has had sufficient experience with a given patient. Adrenaline should be available for treatment of any acute anaphylactoid reaction.

When medicines are made from human blood or plasma, certain measures are put in place to prevent infections being passed on to patients. These include careful selection of blood and plasma donors to make sure those at risk of carrying infections are excluded, and the testing of each donation and pools of plasma for signs of virus/infections. Manufacturers of these products also include steps in the processing of the blood or plasma that can inactivate or remove viruses. Despite these measures, when medicines prepared from human blood or plasma are administered, the possibility of passing on infection cannot be totally excluded. This also applies to any unknown or emerging viruses or other types of infections.

The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus, and for the non-enveloped hepatitis A virus.

The measures taken may be of limited value against non-enveloped viruses such as parvovirus B19.

Immunoglobulins have not been associated with hepatitis A or parvovirus B19 infections possibly because the antibodies against these infections, which are contained in the product, are protective.

It is strongly recommended that every time you receive a dose of Flebogamma® 5% DIF the name and batch number of the product are recorded in order to maintain a record of the batches used.

Interactions and incompatibilities

Flebogamma® 5% DIF administration may impair for a period of at least 6 weeks and up to 3 months the efficacy of live attenuated virus vaccines such as measles, rubella, mumps and varicella.

After injection of Flebogamma® 5% DIF the transitory rise of the various passively transferred antibodies in the patients blood may result in misleading positive results in serological testing.

Incompatibilities

Flebogamma® 5% DIF should not be mixed with any other drugs or intravenous solutions. It should be administered by a separate intravenous line.

Warnings

Pregnancy and lactation

The safety of this medicinal product for use in human pregnancy has not been established in controlled clinical trials and therefore should only be given if clearly indicated to pregnant women and breast-feeding mothers. Long lasting clinical experience with immunoglobulins, indicates that no harmful effects on the course of pregnancy, on the foetus and the neonate are to be expected.

Effects on ability to drive

Not applicable.

Posology

The dose and dosage regimen is dependent on the indication.

In replacement therapy the dosage may need to be individualised for each patient dependent on the pharmacokinetic and clinical response. The following dosage regimens are given as a guideline:

Replacement therapy in primary immunodeficiency syndromes

The dosage regimen should achieve a trough level of IgG (measured before the next infusion) of at least 4 - 6 g/l. Three to six months are required after the initiation of therapy for equilibration to occur. The recommended starting dose is 0.4 - 0.8 g/kg followed by at least 0.2 g/kg every three weeks.

The dose required to achieve a trough level of 6 g/l is of the order of 0.2 - 0.8 g/kg/month. The dosage interval when steady state has been reached varies from 2 - 4 weeks.

Trough levels should be measured in order to adjust the dose and dosage interval.

Idiopathic Thrombocytopenic Purpura

For the treatment of an acute episode, 0.8 - 1 g/kg on day one, which may be repeated once within 3 days, or 0.4 g/kg daily for two to five days. The treatment can be repeated if relapse occurs.

Kawasaki Disease

1.6 - 2.0 g/kg should be administered in divided doses over two to five days or 2.0 g/kg as a single dose.

Patients should receive concomitant treatment with acetylsalicylic acid.

The dosage recommendations are summarised in the following table:

Indication	Dose	Frequency
Replacement therapy in primary immunodeficiency	- starting dose: 0.4 - 0.8 g/kg - thereafter: 0.2 - 0.8 g/kg	every 2 - 4 weeks to obtain IgG trough level of at least 4 - 6 g/l
Immunomodulation: Idiopathic Thrombocytopenic Purpura	0.8 - 1 g/kg or 0.4 g/kg/d	on day 1, possibly repeated once within 3 days for 2 - 5 days
Kawasaki disease	1.6 - 2 g/kg or 2 g/kg	in several doses for 2 - 5 days in association with acetylsalicylic acid in one dose in association with acetylsalicylic acid

Instructions for use

The product should be warmed to room temperature or body temperature before administration.

Flebogamma® 5% DIF should be infused intravenously at an initial rate of 0.01 - 0.02 ml/kg/min. during the first 30 minutes. If well tolerated, the rate of administration may be increased to 0.04 ml/kg/min. and if tolerated subsequent infusions to the same patient may be at this rate. If adverse effects occur the rate should be reduced or the infusion interrupted until the symptoms subside. The infusion may then be resumed at a rate which is tolerated by the patient.

Overdose

Consequences of overdosage are not known since overdosage cases have not been reported.

Undesirable effects

Clinical investigations have confirmed that Flebogamma® 5% DIF is well tolerated and not likely to produce side effects when infused at the recommended rates. However, the first infusion of immunoglobulin particularly in previously untreated agamma- and hypogammaglobulinaemic patients or patients who have previously received another immunoglobulin preparation may lead to systemic side effects. Some of the effects may occur as a result of a reaction between the antibodies administered and free antigens in the blood and tissues of the patient.

Adverse reactions may include flushing of the face, tightness of the chest, chills, fever, dizziness, nausea, mild back pain and hypotension. As with other intravenous immune globulin preparations, Flebogamma® 5% DIF has been associated at high doses with rare occurrences of aseptic meningitis and haemolytic anaemia.

If any adverse reaction, not enclosed in this item, appears, inform your physician or pharmacist.

Storage

Do not store above 30 ºC. Do not freeze.

Any unused solution must be discarded because of bacterial contamination risk.

Keep out of the reach and sight of children.

Shelf-life

Expiry date of the product is stated on the label.

Do not use after expiry date.

Sizes

Flebogamma® 5% DIF 0.5 g, 2.5 g, 5 g, 10 g and 20 g.

This product is restricted for physician use.

Manufacturer

Instituto Grifols, S.A.
Polígono Levante c/Can Guasch, 2
08150 Parets del Vallès, Barcelona-SPAIN

Distributor

Taiwan Green Cross Co., Ltd
6th Floor, No. 244, Sector 3,
Chengteh Road, Taipei, Taiwan R.O.C.

“基立福” 人免疫球蛋白靜脈注射液5%DIF

FLEBOGAMMA® 5% DIF

0.5 · 2.5 · 5 · 10 · 20g

HUMAN NORMAL IMMUNOGLOBULIN FOR INTRAVENOUS USE

Solution for infusion

許可證字號：衛署菌疫輸字第000672號

1. 含human immune globulin成分藥品可能發生血栓。
2. 血栓的危險因子包括：高齡、長時間不活動、血液過度凝集的狀態、具靜脈或動脈血栓病史、使用雌激素、裝有留置型的中央靜脈導管、患血液高度黏稠之疾病及具心血管危險因子。
3. 無已知血栓危險因子者亦可能發生血栓。
4. 具血栓風險的病人，應以最低有效劑量及適當的最小輸注速率投予含human immune globulin成分藥品。
5. 投予前應確保病人有足夠的水分。
6. 具血液高度黏稠風險的病人，應監測血栓相關徵兆及症狀並評估血液之黏稠度。

成　份

	0.5g	2.5g	5g	10g	20g
● 主成分					
Human normal immunoglobulin	0.5g	2.5g	5g	10g	20g
● 賦形劑					
D-Sorbitol					
Water for injection q.s.	10ml	50ml	100ml	200ml	400ml

經放射性免疫擴散法測定IgG亞型（Subclass）即IgG1、IgG2、IgG3、IgG4含量百分比分別約為68.7%、25.9%、3.7%及1.78%。

IgA含量低於0.05mg/ml。

劑型及含量

每公升含50g人免疫球蛋白之注射用溶液。

活　性

本品係由人類血漿中分離出來之未經修飾之免疫球蛋白注射液。

適 應 症

本品適用於:

免疫球蛋白缺乏症。

原發性血小板減少紫癜症。

川崎氏症 (Kawasaki disease)。

禁　忌

- **對於同種免疫球蛋白無耐性者，尤其罕見之IgA缺乏病例，此時病人會產生IgA抗體。**
- **對其它成分有過敏反應者。**

使用 注意

「血栓：使用含human immune globulin成分藥品治療可能發生血栓。危險因子包括：高齡、長時間不活動、血液過度凝集的狀態、具靜脈或動脈血栓病史、使用雌激素、裝有留置型的中央靜脈導管、患血液高度黏稠之疾病及具心血管危險因子。無已知危險因子者亦可能發生血栓。具血液高度黏稠風險的病人，包括：具冷凝球蛋白、空腹乳糜微粒血症/顯著的高三酸甘油脂或單株伽瑪球蛋白症者，應考慮進行血液黏度之基線評估。具血栓風險的病人，應以最低有效劑量及適當的最小輸注速率投予本品。投予前應確保病人有足夠的水分。具血液高度黏稠風險的病人，應監測血栓相關徵兆及症狀並評估血液之黏稠度。」

曾未接受過球蛋白治療或與上次治療時間隔8周以上之球蛋白缺乏或過少症之病人，在注射本品時可能發生炎症反應。此種反應之出現與注射速率相關。反應之表現為體溫上升、惡寒、噁心、嘔吐。應連續監視緊要徵象，並在注射時小心觀察病人。

在醫師對病人有足夠的經驗之前，應遵照"使用方法"中所記載之注射速率。處理急性過敏性反應可用腎上腺素。

經由人類血液或血漿做成之藥物，已設入某些措施以避免感染病人，這包括小心選擇血液及血漿捐贈者以確保排除帶原者感染之危險性，及檢驗每一批捐血及血漿池之病毒感染風險。這些產品的製造廠商在血液或血漿製造過程也進行病毒去活化或移除。儘管已使用上述措施，投予人類血液或血漿製劑之病人仍然無法完全排除任何未知或剛顯露病毒或其他類型感染之可能性。

上述措施對於排除如人類免疫缺乏症病毒(HIV)、B型及C型肝炎病毒之包膜型病毒，和非包膜型之A型肝炎病毒被認為有效。而對於非包膜病毒如parvovirus B19之排除效果可能有限。

關於免疫球蛋白未曾感染A型肝炎或parvovirus B19，可能是因為產品所含抗體產生對抗而達到保護作用。

鄭重建議每次使用本產品時，需記錄本品品名及產品批號以確保使用批號完整記錄。

相互作用及配合禁忌

本品給藥至少6週乃至3個月內可能削弱麻疹、風疹、流行性腮腺炎、水痘等活菌疫苗之功效。投與本品後，病人血中被動輸入之各種抗體效價暫時上升，可能影響血清檢驗結果為陽性。

● 配合禁忌

本品不可與其它任何藥物或靜脈注射輸液混合使用，應單獨使用靜脈注射途徑給藥。