

12 PLASMA DERIVED BLOOD COMPONENTS

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12.18 Flebogamma
Section 12
Transfusion Medicine Protocols
Women's & Newborn Health Services
Perth Western Australia

12.18 FLEBOGAMMA 5% DIF®

DESCRIPTION

Flebogamma 5% DIF® (dual inactivation plus nanofiltration) is a human intravenous immunoglobulin (IVIg) solution. It is a sterile, clear/slightly opalescent and colourless to pale yellow, liquid preparation of immunoglobulin (IgG) obtained from human plasma pools. It contains 50g/L of human normal Immunoglobulin (IgG).

The purification process includes cold alcohol fractionation, polyethylene glycol precipitation, ion exchange chromatography, low pH treatment, pasteurisation, solvent detergent treatment and two sequential nanofiltrations through 35 nm and 20 nm pore size nanofilters connected in series.

In the final formulation, **Flebogamma 5% DIF®** contains 5 g human normal immunoglobulin and 5 g sorbitol (as stabiliser) in 100 ml of water for injections. There is no preservative in the formulation.

Flebogamma 5% DIF® is a highly purified ($\geq 97\%$ IgG), unmodified, human IgG that contains the antibody specificities found in the donor population. IgG subclasses are fully represented with the following approximate percents of total IgG: IgG1 is 66.6%, IgG2, 28.5%, IgG3, 2.7%, and IgG4, 2.2%. It contains only trace amounts of IgA (lower than 0.05 mg/ml).

It is available in 2.5g (50 mL), 5g (100mL) and 10g (200mL) vials.

Further information is available at

<http://www.lateralgrifols.com/index.html>

http://www.transfusion.com.au/blood_products/fractionated_plasma/IVIg#IVIg_flebogamma

Flebogamma is issued on a named patient basis only and is ordered through the Blood Bank. It is supplied by the Australian Red Cross Blood Service (ARCBS) after ARCBS Haematologist Approval.

For new patients, one off approvals OR where each dose requires ARCBS Haematologist approval, an 'ARCBS IVIG Patient Information Form' will be supplied to the requesting Clinician. The Transfusion Medicine Scientist will ask the requestor to specifically class the IVIg indication category as either *a) Haematological b) Neurological or c) Immunological/General*. The relevant form (a, b or c) will then be supplied for completion by the Clinician. Clinicians must complete one form per treatment plan or one-off order. A new form is required if the dose or frequency of infusion changes. *The completed form **must** be returned to the Transfusion Medicine Unit **before** the product can be ordered*

For regular patients a "Weekly Infusion Schedule for Regular Intravenous Immunoglobulin Patients" form may be used. The TM Scientist will fax this form to ARCBS to order approved doses for multiple patients for infusion the following week.

INDICATIONS

Flebogamma 5% DIF® is registered in Australia for the treatment of a limited number of diseases where immunoglobulin replacement or immune modulation therapy is indicated.

The *Criteria for the Clinical Use of Intravenous Immunoglobulin (IVIg) in Australia* has been developed to assist clinicians and transfusion medicine professionals to identify the conditions and circumstances for which the use of intravenous immunoglobulin (IVIg) is appropriate and funded under the National Blood Agreement (NBA). As such **Flebogamma** is available through the Blood Bank and funded through the cost shared arrangements of the National Blood Agreement for approved indications. The “Criteria for the clinical use of intravenous immunoglobulin in Australia” 2007 is available at <http://www.nba.gov.au/iviq/pdf/criteria.pdf>

PRECAUTIONS

- Hereditary Fructose intolerance (contains sorbitol). Special precautions should be taken with babies and young children because this fructose intolerance may be not yet diagnosed and may be fatal.
- Patients with total IgA deficiency.
- There is clinical evidence of an association between IVIg and thromboembolic events that is assumed to be related to a relative increase in blood viscosity through the high influx of immunoglobulin in at risk patients. Caution should be exercised in prescribing IVIg in patients with pre-existing risk factors for thrombotic events.
- Cases of acute renal failure have been reported in patients receiving IVIg therapy.
- Caution must be used if administering the product for the first time or if the patient has had a reaction previously.
- Live vaccine should not normally be given until three months after a dose of gammaglobulin injection. If a live virus vaccine has been given, gammaglobulin should not be given for at least two weeks except in exceptional circumstances. Contact the Clinical Immunologist for advice.
- Patients receiving regular gammaglobulins should have six monthly monitoring of liver function.
- Side effects may include headache, nausea, vomiting, chest tightness, flushing, coughing and chills. If side effects occur – reduce the rate by half and contact the MO
- Refer severe reactions to the Consultant Haematologist unless the patient is under the care of the PMH Department of Immunology in which case refer to the Consultant Immunologist.
- Refer to the Product Information for further details

ADMINISTRATION

- Ensure positive patient identification and ‘Right product to Right patient’ as per hospital transfusion protocols
- Ensure patent IV access
- Ensure solution is clear without any sediment or particles. If the Product appears turbid or contains sediment it must not be used. Return to the Blood Bank.
- Bring Flebogamma 5% DIF® to room temperature before administration.
- Prime the line with Flebogamma 5% DIF®
- Administer through a standard IV infusion set via an infusion device. An in-line filter is not necessary; however, if there is a filter already in an infusion line it will not pose any problems.
- It should be used immediately after opening the bottle as it contains no antimicrobial preservative. Do not use after the expiry date.
- Do not mix this product with other medications or IV fluids.
- Dosage varies and depends on the clinical indication and the age of the patient. If advice is required refer to Clinical Immunologist or Haematologist.
- Refer to the Infusion Rate Guide
- Flush line with saline after completion.
- The product should only be used for the patient for whom it was issued. Any unwanted vials **MUST** be returned to the Blood Bank as soon as possible. Unused vials must not be kept on the ward for allocated patients OR reallocated to other patients.

CHILD INFUSION RATES

Rate is weight-based. Administration is started slowly and increased steadily if no adverse events are noted. Below are examples of infusion rates. A simple conservative approach within the limits of the current product information is listed.

CHILD WEIGHT BASED RATES		
Length of time to infuse	Rate per Hour	
30 minutes	0.5 mL/kg/hr	
30 minutes	1.0 mL/kg/hr	
30 minutes	2.0 mL/kg/hr	
30 minutes	4.0 mL/kg/hr	
30 minutes	6.0 mL/kg/hr	Maximum of 480 mL/hr

ADULT INFUSION RATES

Rate is weight-based. Administration is started slowly and increased steadily if no adverse events are noted. Below are examples of infusion rates.

PATIENTS WEIGHT 40 - 50kg			PATIENTS WEIGHT 50 - 60kg		
Length of time to infuse	Rate per Hour	Volume to be infused	Length of time to infuse	Rate per Hour	Volume to be infused
15 minutes	25 mL / hour	6 mL	15 minutes	30 mL / hour	8 mL
30 minutes	50 mL / hour	25 mL	30 minutes	60 mL / hour	30 mL
30 minutes	100 mL / hour	50 mL	30 minutes	120 mL / hour	60 mL
30 minutes	170 mL / hour	85 mL	30 minutes	210 mL / hour	105 mL
until completed	240 mL / hour	Remainder	until completed	300 mL / hour	Remainder

PATIENTS WEIGHT 60 - 70kg		
Length of time to infuse	Rate per Hour	Volume to be infused
15 minutes	40 mL / hour	10 mL
30 minutes	70 mL / hour	35 mL
30 minutes	140 mL / hour	70 mL
30 minutes	250 mL / hour	125 mL
until completed	300 mL / hour	Remainder

PATIENTS WEIGHT 70 - 80kg			PATIENTS WEIGHT > 80kg		
Length of time to infuse	Rate per Hour	Volume to be infused	Length of time to infuse	Rate per Hour	Volume to be infused
15 minutes	40 mL / hour	10 mL	15 minutes	50 mL / hour	12 mL
30 minutes	80 mL / hour	40 mL	30 minutes	100 mL / hour	50 mL
30 minutes	170 mL / hour	85 mL	30 minutes	190 mL / hour	85 mL
30 minutes	290 mL / hour	145 mL	30 minutes		
until completed	300 mL / hour	Remainder	until completed	300 mL / hour	Remainder

NOTE: Consideration should be given to reducing the rate of infusion in elderly patients and in patients with pre-existing renal disease

PATIENT MONITORING

Take observations as for all blood products, Close observation is required and the patient's general status should be monitored regularly throughout the infusion.

- Record patient's observations:
 - Baseline TPR and BP
 - Repeat 15 minutes post commencement
 - Then after each rate change
 - Then hourly and on completion

After the infusion is complete flush the line with sodium chloride 0.9%

Continue to observe the patient for adverse reactions for 2 hours before discharging them. However, patients on regular gammaglobulin infusions may be discharged on completion if their observations are stable.

If side effects occur reduce the rate by half and contact the MO.

Refer severe reactions to the Consultant Haematologist unless, the patient is under the care of the PMH Department of Immunology, in which case refer to the Consultant Immunologist.

- Adverse reactions tend to be rate related.
- Signs and Symptoms may include: dyspnoea, wheezing, chest tightness, coughing, changes in blood pressure, tachycardia, flushing, fever, rigors, skin rash/urticaria, headache, vomiting, nausea and abdominal and back pain.
- Rarely human normal immunoglobulins may cause a fall in blood pressure and, in isolated cases, anaphylactic shock, even when the patient has shown no previous hypersensitivity.
- Cases of reversible aseptic meningitis, isolated cases of reversible haemolytic anaemia/haemolysis, reversible transient increases in liver transaminases, and rare cases of regressive cutaneous reactions, often eczema-like, have been observed with human normal immunoglobulin.

DOCUMENTATION

A record should be kept in the patient's history of the following

- The date of infusion
- Patients observations and general condition during the infusion
- Amount given
- The batch number and expiry date of each bottle used (place a sticker with the batch number on the Transfusion Medicine Record sheet (KEMH MR735). This information is important should the patient have a reaction to the infusion or if there is a need to trace recipients of certain batch numbers at a later date.

FURTHER INFORMATION

<http://www.transfusion.com.au/sites/default/files/Flebogamma-PI.pdf>

<http://www.transfusion.com.au/sites/default/files/Flebogamma-Infusion-Rate-Calculator.pdf>

BloodSafe Guide to Administration Flebogamma 5% DIF®: Human immunoglobulin solution for infusion accessed via quick links at <http://www.health.sa.gov.au/bloodsafe/Default.aspx?tabid=68>