Immunoglobulin (Flebogamma DIF 10%) Intravenous for Adults

Who can administer

May be administered by registered competent doctor or nurse/midwife

Important information

- Use Online Dosage Calculator and Order Form- only accessible via HSE computer (GUH useful resources- Pharmacy Medicines Information)
- Please ensure you are using correct monograph- separate monographs for **both** Flebogamma DIF **5% and 10%** are available
- **Use 10% Flebogamma DIF** unless instructed by Dr V Tormey and supply of the 5% can be arranged by pharmacy
- **Contraindicated** in individuals with known **class specific antibody to Immunoglobulin A**
- **Thromboembolism:** Use caution with IVIg in **obese patients** and in patients with **pre-existing risk factors for thrombotic events**. In patients at risk for thromboembolic adverse reactions, IVIg products should be administered at the **minimum rate of infusion and dose practicable**
- See **'Monitoring requirements'** below
- This is a **blood product**, therefore batch and expiry information should be recorded in the patient's notes. This is facilitated by putting the dispensing label from each vial into the patient's notes.
- Licensed doses vary with the brand of immunoglobulin employed. Discuss with your consultant or pharmacy if further information required.
- **Glass bottle precautions as follows:**
- Precautions need to be taken during administration to prevent possible air embolism - particularly in central line administration. Bottles must be vented in one of two ways:
    - Directly by means of a filter needle into the bottle which goes through the rubber stopper and opens into the air,
    - or by direct air vent on the air inlet of the administration set, located between the drip chamber and piercing pin, it is covered with a bacterial retentive filter to reduce the chance of contamination

Available preparations

Flebogamma DIF 10% contains human normal immunoglobulin 5g in 50ml

Flebogamma DIF 10% contains human normal immunoglobulin 10g in 100ml

Flebogamma DIF 10% contains human normal immunoglobulin 20g in 200ml

Reconstitution

Already in solution

Infusion fluids

Not required (product ready for infusion)

Methods of intravenous administration

Intermittent intravenous infusion (administer using an electronically controlled infusion device)

- First 30 minutes: 0.6ml/kg/hour
- If well tolerated, the rate may be increased **every 30 minutes in the following step-wise fashion**: 1.2ml/kg/hour, then 2.4ml/kg/hour, then 3.6ml/kg/hour, and finally the maximum rate of 4.8ml/kg/hour.
- It has been reported that the frequency of adverse reactions to IVIg increases with the infusion rate. For patients experiencing adverse reactions it is advisable to reduce the infusion rate in subsequent infusions and limit the maximum rate to 2.4ml/kg/hr or administer IVIG at a 5% concentration.
- When prescribed as a daily dose for several days, the rate will need to be titrated again on each day. However, if it was well tolerated the previous day, the rate may be increased more quickly on subsequent days. (ref 1)
- If prescribed as a daily dose, and on day one it is first administered late in the day, on subsequent days the starting time for administration may be brought back to earlier in the day if required. Gradual titration of the rate will be needed on each day, as before.

Infusion rates for FLEBOGAMMA 10%- sample calculations. See above for exceptions to rate increases

If a patient's weight falls between two values below, use the lower infusion rate- e.g. patient weight 59kg- use rates for 55kg rather than for 60kg

Increase rate as per table below, every 30 minutes as tolerated - <u>until the full dose has been administered</u>

Maintain low rate of infusion throughout if patient has acute renal disease, or thromboembolic disorders

Weight (kg)	First 30 minutes (ml/hour)	Second 30 minutes (ml/hour)	Third 30 minutes (ml/hour)	Fourth 30 minutes (ml/hour)	Maximum rate(ml/hour)
	0.6ml/kg/hour	1.2ml/kg/hour	2.4ml/kg/hour	3.6ml/kg/hour	4.8ml/kg/hour
50	30	60	120	180	240
55	33	66	132	198	264
60	36	72	144	216	288
65	39	78	156	234	312
70	42	84	168	252	336
75	45	90	180	270	360
80	48	96	192	288	384
85	51	102	204	306	408
90	54	108	216	324	432

95	57	114	228	342	456
100 (max weight to use for RATE calculations*)	60	120	240	360	480

* **max 100kg used to calculate dose RATE** - based on requirement not to overload heavy patients with high rate of large volume infusions

Dose in adults

Important points (ref 2)

- Use Online Dosage Calculator and Order Form
- Using this adjusted weight dose may contribute to minimisation of side-effects and will also save significant quantities of immunoglobulin

Replacement therapy in primary immunodeficiency

- 0.4g to 0.8g/kg initially, followed by 0.2g to 0.8g/kg every three to four weeks thereafter, depending on the clinical response and on the IgG trough level.
- Desired trough levels (taken before the next infusion) are at least 6g/L
- Three to six months are required after initiation of therapy for steady-state IgG levels to occur

Replacement therapy in secondary immunodeficiency

- 0.2g to 0.4g/kg every three to four weeks thereafter, depending on the clinical response
- 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

- 0.4g/kg daily for two to five days
- Alternative regimen: 0.8g/kg to 1g/kg on day 1, which may be repeated once within three days if relapse occurs

Guillain Barre syndrome

- 0.4g/kg daily for 5 days
- possible repeat of dosing in case of relapse

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

- **Starting dose:** Give 2g/kg given over two to five days .(example 1g/kg daily for two days, or 0.4g/kg daily for five days)
- **Maintenance dose:** Give 1g/kg given over one to two days, every three weeks

Multifocal Motor Neuropathy (MMN)

- **Starting dose:** Give 2g/kg given over two to five days (example 1g/kg daily for two days, or

0.4g/kg daily for five days)
- **Maintenance dose:** Give 1g/kg every two to four weeks, **or** 2g/kg every four to eight weeks over 2 to 5 days
- Treatment effect should be evaluated after each cycle. If no response after six months, then treatment should be discontinued

Measles prophylaxis [ref 3](see NIAC Immunisation Guidelines, Chapter 12, Measles)

- Give 0.4g per kg stat
- For example 0.4g per kg for patient who weighs 65kg is 26g - give 25g (2x10g vials + 5g vial)
- If there is significant ongoing or re-exposure to measles following the administration of IVIG, the administration should be repeated at three weekly intervals

See SPC for other indications

Monitoring

- Patients must be **closely monitored** and carefully observed for any adverse reactions throughout the infusion period and for **at least 20 minutes** after administration
- **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**
- Monitoring should be **extended to 60 minutes for immunoglobulin naive patients**, those **switched** from another product, or when there has been a **long interval** since previous infusion.
- If adverse reactions occur, slow or stop the infusion - see under 'Further information'. Please also consult Medication Protocol: Management of Infusion Related patient reactions in nurse led infusion settings in GUH -available on Q pulse (CLN-NM-0118)
- For patients who experience adverse reactions, it is advisable to reduce the rate of subsequent infusions to a maximum rate of 2.4ml/kg/hour, or administer the 5% concentration
- Ensure the following when administering IVIG
    - adequate hydration prior to the initiation of the infusion of IVIg
    - monitoring of urine output
    - monitoring of serum creatinine levels
    - monitoring for signs and symptoms of thrombosis
    - assessment of blood viscosity in patients at risk for hyperviscosity
    - avoidance of concomitant use of loop diuretics

Further information

- **Management of infusion related reactions:** depending on the severity of the reactions, the infusion rate may either be **slowed or stopped**.
- Some cases of **acute renal failure** have been reported in patients receiving IVIG
    - This is particularly those containing sucrose as an excipient (Flebogamma does not contain sucrose)
    - administer at the minimum rate of infusion and dose practicable for patients at risk for acute renal failure
- Contains 50mg/ml **sorbitol** as an excipient. Should not be administered to patients with rare hereditary problems of **fructose** intolerance
- IVIG may interfere with responses to **live vaccines** - serological testing may be necessary- see SPC for details
- IgA content is less than or equal to 100 microgam per ml

- IgG content is at least 97%

Storage

Store below 25^{0}C

Do not freeze

References

Summary of Product Characteristics Flebogamma Dif 24/4/2017

(1) Communication with Dr Tormey, immunologist, email March 2011

(2) Department of Health UK 2011 Clinical guidelines for the use of intravenous immunoglobulins 2nd edition update

3. NIAC immunisation guidelines Measles Prophylaxis- see page 19

Therapeutic classification

Intravenous immunoglobulin