Guidelines – Standardised infusion rates for IVIg (intravenous immunoglobulin) replacement therapy

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Immunoglobulin replacement therapy (IRT) is the standard treatment for most children and adults with primary immune deficiencies and some other medical conditions. The aim is to replace immunoglobulin to maintain normal IgG levels. The dose used is individualised for each patient. IRT may be given as intravenous immunoglobulin (IVIg) or subcutaneous immunoglobulin (SCIg).

When prescribing IVIg or SCIg, you must ensure that doses are rounded to the full vial size. Immunoglobulin is a plasma derived product and is a limited resource. Prescribing a dose that uses a partial vial can result in unnecessary wastage. Vial sizes vary between different products, and this must be taken into account before prescribing.

There are several intravenous immunoglobulin (IVIg) immunoglobulin products available. In both Australia and New Zealand, the IVIg products imported for clinical use may change from time to time.

Products that are currently available include:

- **Intragam® 10 (CSL Behring)** - 10% w/v solution of IgG produced from voluntary donors to the Australian Red Cross LifeBlood service. Intragam® 10 is available in 2.5g in 25 ml, 10g in 100 ml and 20g in 200 ml. This product is being phased out in 2023 and will be replaced with **Privigen AU®**.
- **Privigen AU® (CSL Behring)** - 10% solution of IgG produced from voluntary donors to the Australian Red Cross LifeBlood service. Privigen AU® is available in 5g in 50 ml, 10g in 100ml, and 20g in 200ml.
- **Privigen® (CSL Behring)** - 10% solution of IgG derived from imported plasma, available in 5g in 50 ml, 10g in 100ml, 20g in 200ml and 40g in 400 ml.
- **Flebogamma® (Grifols)** - available in both 5% and 10% solutions of IgG derived from imported plasma. Flebogamma® 5% is available in 0.5 g in 10 ml, 2.5 g in 50 ml, 5 g in 100 ml, 10 g in 200 ml and 20g in 400 ml. Flebogamma® 10% is available in 5 g in 50 ml, 10 g in 100 ml and 20 g in 200 ml.
- **Gamunex® (Grifols)** - 10% solution of IgG derived from imported plasma, available in 5g in 50 ml, 10g in 100ml and 20g in 200ml.
- **Kiovig® (Takeda)** - 10% solution of IgG derived from imported plasma, available in 1g in 10 ml, 2.5g in 25ml, 5g in 50ml, 10g in 100ml and 20g in 200ml.
- **Octagam® (Octapharma)** - 10% solution of IgG derived from imported plasma, available in 5g in 50 ml, 10g in 100ml and 20g in 200ml.

Infusion Rates

Individual products recommend different weight-based rates of infusion. To avoid confusion, ASCIA has developed standardised infusion rates for both 5% and 10% solutions, regardless of product. These rates are generally well tolerated.

These recommended infusion rates are for patients with immune deficiency on replacement IVIg therapy. Patients using IVIg for other conditions such as Kawasaki disease or immunomodulation should follow local protocols.

Adverse reactions

Adverse reactions can be related to the rate of infusion and often resolve with stopping or slowing the infusion rate. However, a medical review may be required before re-starting the infusions to rule out other pathologies.

Severe reactions are uncommon and are most likely to occur during the first infusion, but may also occur subsequently. Symptoms or signs of reactions 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.

The following guide may be followed when adverse reactions occur.

In response to a minor reaction (flushes, nausea, back or abdominal pain, dizziness and headache):

- Stop infusion immediately.
- Report any adverse effects immediately to the supervising medical officer and nurse and request medical review.
- Once the patient is stable, consider administration at a slower rate. Adverse reactions are usually dependent on the infusion rate and most commonly occur in the first hour of infusion.
- A reduction in maximum infusion rate may be required if post infusion symptoms such as headache or myalgia occur.
- If the reaction persists or the patient does not tolerate further administration, report the reaction, contact the product manufacturer, and notify ARCBS or NZBS, including product batch number.

In response to a severe allergic reaction (anaphylaxis) with respiratory or cardiac compromise:

- Stay with patient.
- Stop infusion immediately, maintaining patency of intravenous access.
- Administer oxygen.
- Implement medical emergency procedure.
- Prepare emergency medication for treatment of acute anaphylaxis for administration.
- Continuously monitor airway, breathing, circulation and neurological status (include urine output, volume, and colour).
- Document event on patient medical record.
- Return remaining blood product to pathology with a pathology request form, indicating symptoms the patient experienced and testing required.

First Infusion

10% IVIg products: For the first infusion, **Intragam® 10, Privigen AU®, Privigen®, Flebogamma® 10%, Gamunex®, Kiovig®** and **Octagam® 10%** should be infused at a rate of 0.5 ml/kg/hour for the first 30 minutes. If there are no adverse reactions the rate can be increased every 30 minutes according to the table, up to a maximum rate of 3 ml/kg/hour, but not to exceed **150 ml/hour**.

5% IVIG products: For the first infusion, **Flebogamma® 5%** should be infused at a rate of 1 ml/kg/hour for the first 30 minutes. If there are no adverse reactions the rate can be increased every 30 minutes according to the table, up to a maximum rate of 6 ml/kg/hour, but not to exceed **300 ml/hour**.

		First Infusion	
		10% IVIg products	**5% IVIg products**
		Intragam® 10, Privigen AU®, Privigen®, Flebogamma® 10%, Gamunex®, Kiovig®, Octagam® 10%.	Flebogamma® 5%
Step	Time	Rate (ml/kg/hour)	Rate (ml/kg/hour)
1st	30 minutes	0.5	1
2nd	30 minutes	1	2
3rd	30 minutes	2	4
4th	To complete infusion	3[1]	6[2]

[1] Rate not to exceed 150 ml/hour; [2] Rate not to exceed 300 ml/hour.

Subsequent Infusions

10% IVIg products: If there is no reaction to the first infusion, **Intragam® 10, Privigen AU®, Privigen®, Flebogamma® 10%, Gamunex®, Kiovig®** and **Octagam® 10%** should be infused at a rate of 0.5 ml/kg/hour for the first 15 minutes. If there are no adverse reactions the rate can be increased every 15 minutes according to the table, up to a maximum infusion rate of 3 ml/kg/hour, but not to exceed **300 ml/hour**.

Patients considered at risk with co-morbidities (such as cardiac disease or renal failure) should have a maximum infusion rate of 200 ml/hour.

5% IVIg products: If there is no reaction to the first infusion, **Flebogamma® 5%** should be infused at a rate of 1 ml/kg/hour for the first 15 minutes. If there are no adverse reactions the rate can be increased every 15 minutes according to the table, up to a maximum infusion rate of 6 ml/kg/hour, but not to exceed **500 ml/hour**.

Patients considered at risk with co-morbidities (such as cardiac disease or renal failure) should have a maximum infusion rate of 300 ml/hour.

		Subsequent Infusion	
		10% IVIg products	**5% IVIg products**
		Intragam® 10, Privigen AU®, Privigen®, Flebogamma® 10%, Gamunex®, Kiovig®, Octagam® 10%.	Flebogamma® 5%
Step	Time	Rate (ml/kg/hour)	Rate (ml/kg/hour)
1st	15 minutes	0.5	1
2nd	15 minutes	1	2
3rd	15 minutes	2	4
4th	To complete infusion	3[1]	6[2]

[1] Rate not to exceed 300 ml/hour; [2] Rate not to exceed 500 ml/hour.

This document will next be updated when there are changes in availability of IVIg products.

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