ascia
australasian society of clinical immunology and allergy
www.allergy.org.au
Guidelines
FOR HEALTH PROFESSIONALS

Intravenous Immunoglobulin (IVIg) Replacement Therapy Infusion Rates and Adverse Reactions Guide

This document has been developed by ASCIA, the peak professional body of clinical immunology/allergy specialists in Australia and New Zealand. ASCIA information is based on published literature and expert review, is not influenced by commercial organisations and is not intended to replace specific medical advice. For patient or carer support contact AusPIPS, IDFA, or IDFNZ.

Immunoglobulin replacement therapy (IRT) is a standard treatment for many children and adults with inborn errors of immunity (IEI) requiring antibody replacement.

IRT is given as intravenous immunoglobulin (IVIg) or subcutaneous immunoglobulin (SCIg):

- The aim of IVIg and SCIg is to replace immunoglobulin to maintain normal Immunoglobulin G (IgG) levels and the dose used is individualised for each patient.
- IVIg and SCIg products are manufactured from human plasma and undergo stringent controls to minimise the possibility of pathogen transmission.
- IVIg and SCIg are used to treat some other medical conditions, but these Guidelines are specific for IRT.

In Australia, IVIg and SCIg require authorisation through the National Blood Authority BloodSTAR system.

When prescribing IVIg or SCIg, you should 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 should be taken into account before prescribing.

IVIg products that are currently available in Australia and New Zealand

Local IVIg products - derived from plasma sourced from voluntary donors within Australia (to the Australian Red Cross LifeBlood Service) or within New Zealand (to the New Zealand Blood Service):

- **Privigen AU®** (CSL Behring) - 10% solution of IgG available in 5g in 50 ml, 10g in 100ml, and 20g in 200ml.
- **Privigen NZ®** (CSL Behring) - 10% solution of IgG available in 5g in 50 ml, 10g in 100ml, and 20g in 200ml.

Imported IVIg products - derived from plasma sourced outside of Australia and New Zealand:

- **Privigen®** (CSL Behring) - 10% solution of IgG 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. Flebogamma® 5% is available in 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, available in 5g in 50 ml, 10g in 100ml, 20g in 200ml and 40g (400ml).
- **Kiovig®** (Takeda) - 10% solution of IgG, available in 5g in 50ml, 10g in 100ml, 20g in 200ml and 30g in 300ml.
- **Octagam®** (Octapharma) - 10% solution of IgG, available in 5g in 50 ml, 10g in 100ml and 20g in 200ml.

Products and vial sizes listed above may vary due to National Blood Supply Arrangement changes.

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

IVIg infusion rates

Individual products recommend different weight-based rates of infusion. To avoid confusion, ASCIA has developed tables showing infusion rates for 10% and 5% solutions, which are generally well tolerated.

These recommended infusion rates are for patients with immune deficiencies on replacement IVIg therapy.

Patients using IVIg for other conditions such as Kawasaki disease or immunomodulation should follow local protocols or the rates in the product information (PI).

First IVIg Infusion Use this rate for: • First infusion • Switching between products • Significant gap between infusions		Privigen AU®, Privigen NZ®, Privigen®	Privigen AU®, Privigen NZ®, Privigen®	Flebogamma® 10%, Gamunex®, Kiovig®, Octagam® 10%.	Flebogamma® 5%
Steps	**Time** (increase rate every 30 minutes only if tolerated by patient)	**Rate** (mL/kg/hour) **PI***	**Rate** (mL/kg/hour) **RCH Guideline****	**Rate** (mL/kg/hour)***	**Rate** (mL/kg/hour)***
1	30 minutes	0.3	0.25	0.5	1
2	30 minutes	0.6	0.5	1	2
3	30 minutes	1.2	1.0	2	4
4	30 minutes	2.4	1.5	3	6
5	30 minutes	-	2.0	-	-
6	30 minutes	-	2.5	-	-
		Do not exceed 150 mL/hour			Do not exceed 300 mL/hour

* Infusion rates from the production information (PI) are the same for subsequent infusions (if tolerated)

** Rates are based on RCH VIC IVIg Guideline and specialist consensus from ASCIA members

*** Rates are unchanged from previous ASCIA Guidelines and are the same as RCH VIC IVIg Guidelines

Subsequent IVIg Infusions Only follow if there is no adverse event/reaction to first infusion		Privigen AU®, Privigen NZ®, Privigen®	Privigen AU®, Privigen NZ®, Privigen®	Flebogamma® 10%, Gamunex®, Kiovig®, Octagam® 10%.	Flebogamma® 5%
Steps	**Time** (increase rate every 30 minutes only if tolerated by patient)	**Rate** (mL/kg/hour) **PI***	**Rate** (mL/kg/hour) **RCH Guideline****	**Rate** (mL/kg/hour)***	**Rate** (mL/kg/hour)***
1	30 minutes	0.3	0.5	0.5	1
2	30 minutes	0.6	1.0	1	2
3	30 minutes	1.2	1.5	2	4
4	30 minutes	2.4	2.0	3	6
5	30 minutes	-	2.5	-	-
		Do not exceed 240 mL/hour		Do not exceed 300 mL/hour	Do not exceed 600 mL/hour

Adverse reactions and events during or after IVIg infusions

Recommended infusion rates are generally well tolerated by patients with immune deficiencies on replacement IVIg therapy.

However, side effects of IVIg can occur, including:

- **Acute adverse reactions during or soon after infusions** (e.g. dyspnoea, wheezing, chest tightness, coughing, changes in blood pressure, tachycardia, flushing, fever, rigors, skin rash/urticaria, headache, vomiting, nausea and abdominal and back pain).
- **Delayed adverse events** (e.g. headache and aseptic meningitis).

Adverse reactions and events to IVIg may relate to:

- Higher infusion rates (e.g., >3mL/kg/hr)
- Patients receiving higher doses of IVIg
- Patients naive to IVIg
- Changing from one IVIg product to another
- Long intervals between infusions
- Poor hydration status of patient
- Patients with a history of, or current cerebral oedema
- Patient's risk factors, comorbidities and tolerance to previous infusions

Precautions to minimise adverse reactions and events

Precautions include:

- Assessing patients for adequate hydration prior to IVIg infusion. Consider pre-hydration with IV fluids if clinically required.
- Educating patients to be well hydrated (e.g. oral fluids) in the day leading up to the IVIg infusion.
- Considering pre-medications if prior rate-related reactions to IVIg (e.g. anti-pyretics, anti-emetics, non-sedating antihistamines, oral/IV corticosteroids).
- Assessing renal function in patients with possible renal impairment prior to product commencement.
- Infusing IVIg at the slowest infusion rate possible, for patients with previous severe adverse events to IVIg (e.g. aseptic meningitis, renal failure or thromboembolic events).

Immunisation

IVIg may impair the efficacy of live attenuated vaccines and there are specific deferral periods – refer to the Immunisation Handbook for details.

Contraindications

IVIg infusions are contraindicated in patients who have:

- Had a severe allergic reaction (anaphylaxis) to human immunoglobulins.
- Hereditary fructose intolerance - this applies to Flebogamma 5% and 10% which are contraindicated in babies and young children (up to 2 years of age) who may not yet be diagnosed with this condition, which can be fatal.

This information has been adapted from the RCH VIC IVIg Guideline

Guide to follow when adverse reactions and events occur

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

- Stop IVIg infusion immediately.
- Report any adverse effects immediately to the supervising medical officer and nurse and request medical review.
- Once the patient is stable, consider infusing at a slower rate. Adverse reactions are usually dependent on the infusion rate and most commonly occur in the first hour of infusion.

If post IVIg infusion symptoms such as headache or myalgia occur, one of or a combination of the following measures may be required for subsequent IVIg infusions:

- A reduction in maximum infusion rate
- Appropriate pre-medication
- Adequate hydration prior to infusion

Guide to follow when severe adverse reactions occur

Severe reactions to IVIg are uncommon and are most likely to occur during the first infusion, but may also occur with subsequent infusions.

In response to anaphylaxis with respiratory or cardiac compromise:

- Stop infusion immediately, maintaining patency of intravenous access
- Refer to ASCIA Guidelines - Acute Management of Anaphylaxis
- Return remaining blood product to pathology with a pathology request form, indicating symptoms the patient experienced and testing required.

Reporting of adverse reactions and events

Acute and delayed reactions to IVIg should be reported by notifying the TGA or NZBS:

- Report an adverse event or problem (health professionals) | Therapeutic Goods Administration (TGA)
- Report an adverse event or problem (health professionals) | New Zealand Blood Service (NZBS)

The notifications should also be sent to the **product manufacturer** and the **local institution**.

The **product batch numbers** should always be included in the notifications.

Content updated December 2024

For more information go to www.allergy.org.au/hp/papers/immunodeficiency

To support allergy/immunology research go to www.allergyimmunology.org.au