Intravenous immunoglobulin – 2018

Updated September 2019

Blood Matters and the Victorian Transfusion Nurses (Australian Red Cross Blood Service)

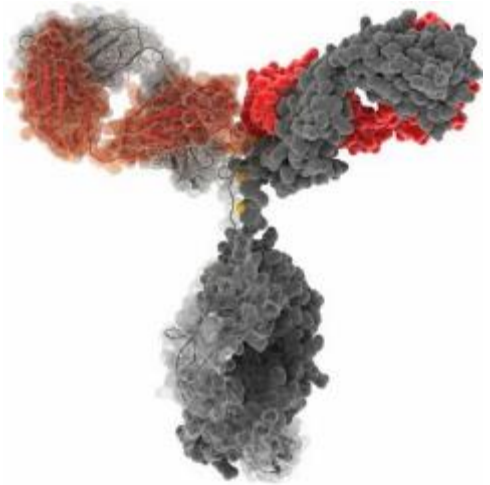


Image Courtesy : upload.wikimedia.org/wikipedia/commons

Background

- Demand for IVIg in Australia continues to grow by more than 10% per annum
- National Blood Authority has put in place a number of things to assist in meeting this demand:
  - Criteria for clinical use – to help ensure it is used only when appropriate
  - BloodSTAR – to manage requests and inventory
  - Importing product to fill shortfall

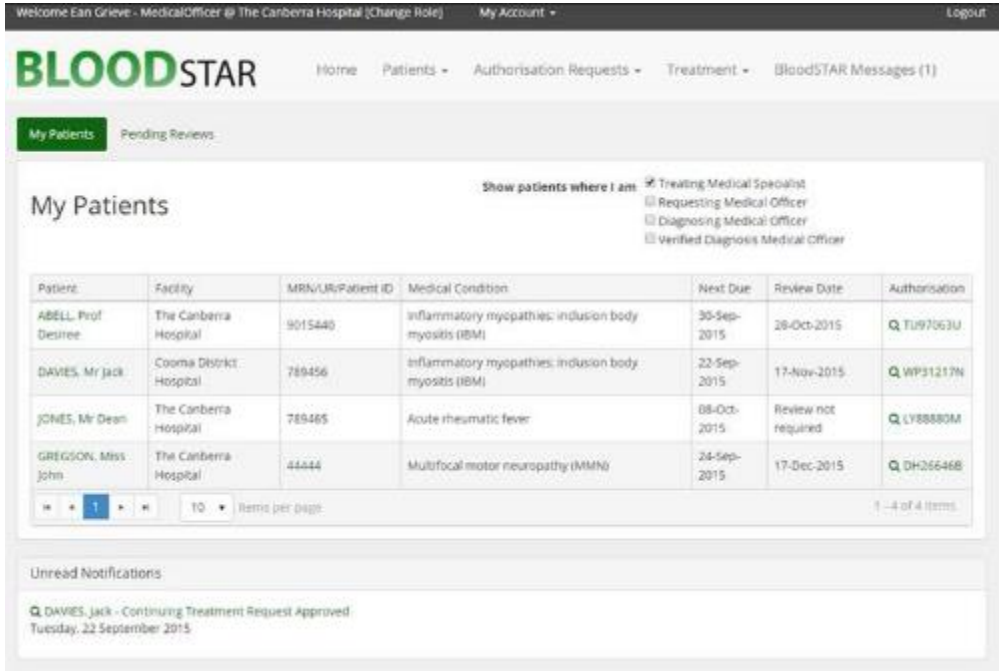
Current supply arrangements

	Current supply arrangements	
Imported IVIg products	Flebogamma® 5%	Grifols Australia
	Flebogamma® 10%	Grifols Australia
	Gamunex® 10%	Grifols Australia
	Privigen® 10%	CSL Behring
Domestic IVIg product	Intragam® 10 (10%)	CSL Behring
Imported SCIg products	Hizentra® 20%	CSL Behring
Domestic SCIg product	Evogam® 16%	CSL Behring

BloodSTAR

Who uses BloodSTAR?

- **Prescribers** – of immunoglobulin products
- **Authorisers** – specified staff of the Australian Red Cross Blood Service
- **Nurses** – who arrange patient treatments
- **Dispensers** – in the course of managing inventory, ordering products and dispensing the correct products to authorised patients



BloodSTAR – view authorisation

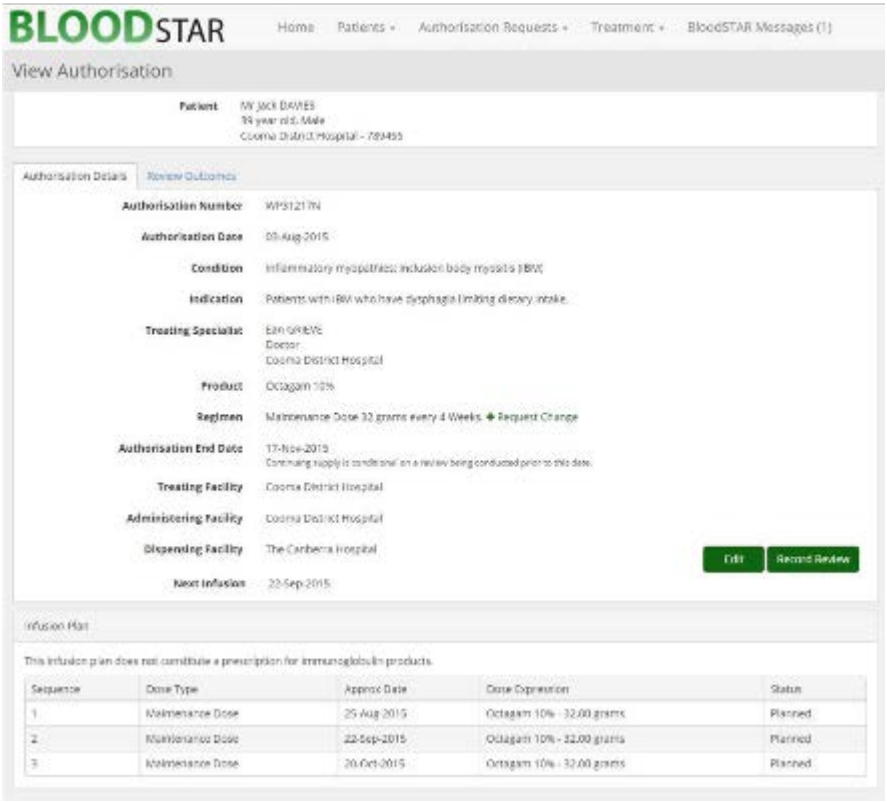
The View authorisation record provides a central point for checking a patients authorised dose and status.

In BloodSTAR:

- Prescribers and nurses can view this for all patients at their facility.
- Medical Officers can also record review outcomes for the patients from this screen.

In BloodNET:

- Dispensers can view the same level of detail using the ‘Check Authorisation’ function.



The prescribing clinician should be contacted for any questions about dose or product.

The Criteria for Immunoglobulin Use in Australia

The Criteria for Immunoglobulin Use in Australia (the Criteria) changed to Version 3, 22 October 2018.

Why did the Criteria Change?

- To align with new evidence
- To ensure those whose health is most likely to be improved with Ig therapy can get it
- To manage the growth in demand for this precious, human-derived product

For more information on the Criteria and the Immunoglobulin Governance program please visit https://www.blood.gov.au/Ig-governance

For the latest Immunoglobulin Governance updates visit https://www.blood.gov.au/Ig-program-updates

BloodSTAR – further information

- For further information on BloodSTAR and its' use you can find this on the National Blood Authority website at https://www.blood.gov.au/bloodstar-support-materials

Authoriser
(Australian Red Cross Blood Service)

Dispenser

Facility Administrator

Call: 13 000 BLOOD

Jurisdictional direct orders (JDOs)

- Medical officers can prescribe IVIg for patients with medical conditions not funded under the Criteria
- The MO can seek funding for IVIg through local arrangements (e.g. local health service therapeutics committee)
- Only imported IVIg is available for purchase under the JDO arrangements
- Imported IVIg can be accessed directly from the supplier at the same price negotiated by the NBA and must be paid for in full by the Approved Recipient (health service or individual patient)

https://www.blood.gov.au/Intravenous-Ig

Intragam® 10

Description	Intragam® 10
Presentation	2.5 g (25 mL), 10 g (100 mL) and 20 g (200 mL) vials
Concentration	10%
Source Plasma	Australia
Stabiliser	Glycine
Storage Condition	• Store at 2°C to 8°C (Refrigerate. Do not freeze). • Once removed from refrigeration, store below 25°C and use within 3 months. • Protect from light.

Intragam® 10 Infusion rate guide (adults)

The infusion rates in the table below are derived from two INTRAGAM 10 clinical studies in adult patients only, with PID and ITP.[2]

		Pump settings	
Infusion phase	Infusion rate‡	mL/hour	Volume infused/time
First 15 minutes	1 mL/min	60 mL/hr	15 mL/15 min
Next 15 minutes	If well tolerated, gradually increase infusion rate over the next 15 minutes to a maximum infusion rate of 3 to 4 mL/min. The rate at which the infusion is increased is at the discretion of the healthcare professional and as tolerated by the patient.		
	For example: 2 mL/min for 5 minutes 3 mL/min for 5 minutes 4 mL/min for 5 minutes	 120 mL/hr 180 mL/hr 240 mL/hr	 10 mL/5 min 15 mL/5 min 20 mL/5 min
Remainder of infusion	Maximum 4 mL/minute	240 mL/hr	Until infusion complete

‡In patients at risk for aseptic meningitis syndrome, migraine, frequent headaches, renal failure, or thromboembolic adverse reactions IVIg products should be administered at the minimum rate of infusion and dose practicable.[2]

https://www.cslbehring.com.au/-/media/cslb-australia/documents/aus-pis-and-cmis/intragam-10-au-pi-800.pdf?la=en-us&hash=9C15DBA43676273478BAE3C1A60AD746FC13D393

FLEBOGAMMA® 5% DIF

NB: Pay careful attention that you have the correct product strength.

Description	FLEBOGAMMA® 5% DIF
Presentation	0.5 g (10 mL), 2.5 g (50 mL), 5 g (100 mL), 10 g (200 mL), 20 g (400 mL) vials
Concentration	5%
Source Plasma	USA and European remunerated and non-remunerated donors
Stabiliser	Sorbitol
Storage Condition	Store below 30°C for up to 2 years, protect from light. Do not freeze.
N.B.	Flebogamma 5% & 10% is contraindicated in babies and young children as hereditary fructose intolerance may not yet be diagnosed and may lead to a fatal reaction associated with the sorbitol stabiliser.

FLEBOGAMMA® 5% DIF infusion rate guide:

Infusion rate		Patient weight (kg)											
mL/kg/min	mL/kg/hr	10	20	30	40	50	60	70	80	90	100	110	120
0.01	0.6	6	12	18	24	30	36	42	48	54	60	66	72
0.02	1.2	12	24	36	48	60	72	84	96	108	120	132	144
0.03	1.8	18	36	54	72	90	108	126	144	162	180	198	216
0.04	2.4	24	48	72	96	120	144	168	192	216	240	264	288
0.05	3.0	30	60	90	120	150	180	210	240	270	300	330	360
0.06	3.6	36	72	108	144	180	216	252	288	324	360	396	432
0.07	4.2	42	84	126	168	210	252	294	336	378	420	462	504
0.08	4.8	48	96	144	192	240	288	336	384	432	480	528	576
0.09	5.4	54	108	162	216	270	324	378	432	486	540	594	648
0.10	6.0	60	120	180	240	300	360	420	480	540	600	660	720

- Increase the rate by 0.01 mL/kg/min (0.6 mL/kg/hr) every 30 minutes to a maximum of 0.10mL/kg/min (6mL/kg/hr) as tolerated by the patient
- This table was developed using the FLEBOGAMMA® 5% DIF product information, always refer to the product information and your local Clinical Practice Guidelines for more information

FLEBOGAMMA® 10% DIF

NB: Pay careful attention that you have the correct product strength.

Description	FLEBOGAMMA® 10% DIF
Presentation	5g (50mL), 10g (100mL), 20g (200mL) vials
Concentration	10%
Source Plasma	USA and European remunerated and non-remunerated donors
Stabiliser	Sorbitol
Storage Condition	Store below 30°C for up to 2 years, protect from light. Do not freeze.
N.B.	Flebogamma 5% & 10% is contraindicated in babies and young children as hereditary fructose intolerance may not yet be diagnosed and may lead to a fatal reaction associated with the sorbitol stabiliser.

FLEBOGAMMA® 10% DIF infusion rate guide:

Infusion Rate		Patient's Weight (kg)											
mL/kg/min	mL/kg/hr	10	20	30	40	50	60	70	80	90	100	110	120
0.01	0.6	6	12	18	24	30	36	42	48	54	60	66	72
0.02	1.2	12	24	36	48	60	72	84	96	108	120	132	144
0.03	1.8	18	36	54	72	90	108	126	144	162	180	198	216
0.04	2.4	24	48	72	96	120	144	168	192	216	240	264	288
0.05	3.0	30	60	90	120	150	180	210	240	270	300	330	360
0.06	3.6	36	72	108	144	180	216	252	288	324	360	396	432
0.07	4.2	42	84	126	168	210	252	294	336	378	420	462	504
0.08	4.8	48	96	144	192	240	288	336	384	432	480	528	576

- Increase the rate by 0.01 mL/kg/min (0.6 mL/kg/hr) every 30 minutes to a maximum of 0.08ml/kg/min (4.8 mL/kg/hr) as tolerated by the patient
- This table was developed using the FLEBOGAMMA® 10% DIF product information, always refer to the product information and your local Clinical Practice Guidelines for more information

Gamunex® 10%

Available from
01/11/2019

Description	Gamunex® 10%
Presentation	5g (50mL), 10g (100mL), 20g (200mL) vials
Concentration	10%
Source plasma	USA and European remunerated and non-remunerated donors
Stabiliser	Glycine
Storage Condition	Store at 2˚C - 8˚C for up to 36 months, may be stored at temperatures not exceeding 25˚C for up to 6 months anytime during the 36 month shelf life, after which the product must be used immediately or discarded. Do not freeze.

Gamunex® 10% infusion rate guide:

Infusion Rate		Patient's Weight (kg)											
mL/kg/min	mL/kg/hr	10	20	30	40	50	60	70	80	90	100	110	120
0.01	0.60	6	12	18	24	30	36	42	48	54	60	66	72
0.02	1.20	12	24	36	48	60	72	84	96	108	120	132	144
0.03	1.80	18	36	54	72	90	108	126	144	162	180	198	216
0.04	2.40	24	48	72	96	120	144	168	192	216	240	264	288
0.05	3.00	30	60	90	120	150	180	210	240	270	300	330	360
0.06	3.60	36	72	108	144	180	216	252	288	324	360	396	432
0.07	4.20	42	84	126	168	210	252	294	336	378	420	462	504
0.08	4.80	48	96	144	192	240	288	336	384	432	480	528	576

- Commence at a rate of 0.01 mL/kg/min for the first 30 minutes
- If well tolerated, the rate may be gradually increased to a maximum of 0.08mL/kg/min
- If side effects should occur, the rate may be reduced, or the infusion interrupted until symptoms subside

This table was developed using the Gamunex® 10% product information, always refer to the product information and your local Clinical Practice Guideline for more information

PRIVIGEN® 10% Solution

Description	PRIVIGEN® 10%
Presentation	5g (50mL), 10g (100mL), 20g (200mL) and 40g (400mL) vials
Concentration	10%
Source Plasma	European and USA remunerated and non-remunerated donors
Stabiliser	Proline (non-essential amino acid)
Storage Condition	Store below 25°C for up to 3 years, protect from light. Do not freeze.

PRIVIGEN® 10% infusion rate guide:

Biotherapies for Life™ CSL Behring

Privigen®: Normal Immunoglobulin (Human) 10% (100 g/L), intravenous injection
Infusion Rate (mL/hr) Calculator†[1–5]

†The infusion calculator below is provided as a guide only. The infusion rate needs to be individualised to the patient's risk factors, comorbidities and tolerability.

Infusion Rate (mL/kg/hr)	Pump rate	Patient's body weight (kg)																	
		10	15	20	25	30	35	40	45	50	55	60	65	70	75	80	85	90	95	100
0.3	mL/hr	3	4.5	6	7.5	9	10.5	12	13.5	15	16.5	18	19.5	21	22.5	24	25.5	27	28.5	30
0.6	mL/hr	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60
1.2	mL/hr	12	18	24	30	36	42	48	54	60	66	72	78	84	90	96	102	108	114	120
2.4*	mL/hr	24	36	48	60	72	84	96	108	120	132	144	156	168	180	192	204	216	228	240
3.6*	mL/hr	36	54	72	90	108	126	144	162	180	198	216	234	252	270	288	306	324	342	360
4.8*	mL/hr	48	72	96	120	144	168	192	216	240	264	288	312	336	360	384	408	432	456	480

*Step rate rises between 2.4 mL/kg/hr and 4.8 mL/kg/hr are at the discretion of the healthcare professional and as tolerated by the patient

Initiation rate[1–4]
0.3 mL/kg/hr

→ **If well tolerated, the rate can be gradually increased** at 30 minute intervals, to a recommended maximum rate[1–4]

→ *

Maximum infusion rate:
PID & CIDP - 4.8 mL/kg/hr (with exception of the first three infusions, where the maximum rate is 2.4 mL/kg/hr)[3,5]
ITP - 2.4 mL/kg/hr[2]

As with all intravenous immunoglobolins (IVIgs) the patient needs to be adequately hydrated prior to being infused and should be closely monitored and carefully observed for any symptoms both during and after the infusion.[1] In patients at risk for acute renal failure, or thromboembolic adverse reactions, IVIg products should be administered at the minimum rate of infusion and dose practicable.[1] In the case of an adverse reaction, the rate of administration must be reduced or the infusion stopped.[1]

PID=Primary Immune Deficiency; CIDP=Chronic Inflammatory Demyelinating Polyneuropath; ITP=Idiopathic

For further information contact CSL Behring

Pre-administration:

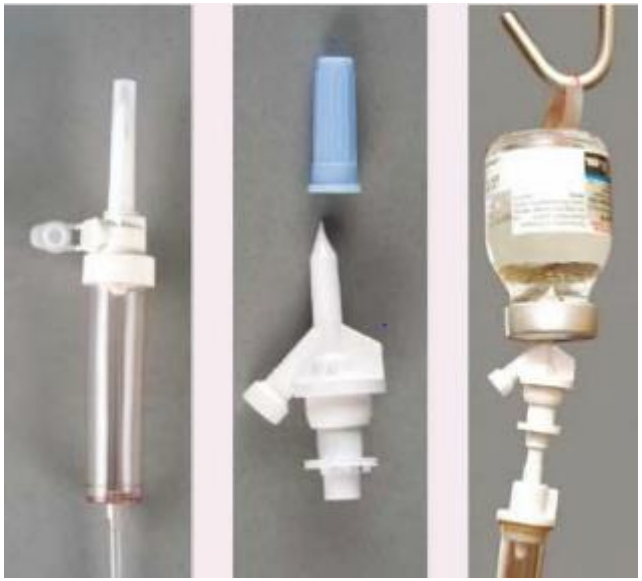
- Document baseline observations
- Assess the patient for signs or symptoms that may be confused with a transfusion reaction
- Hydration – ensure patient is well hydrated as this will help to reduce the risk of some reactions
- Perform pre-administration patient and product identification checks (check local policy)
- Check the integrity of the product
    - All products should be clear or slightly opalescent liquids ranging from colourless to pale yellow
    - Do not use solutions that are cloudy or have deposits

Administration

1. Allow IVIg to come to room temperature before use
2. Remove the plastic cover from the seal
3. Apply a suitable antiseptic (alcohol swab) to the exposed part of the rubber stopper and allow to dry (as per local policy)

NOTE: Administration from glass bottles requires a vented system. A vented system can be in the form of a vented spike adaptor, a side vent in an IV line or an airway needle.

The product does not contain any preservative or antimicrobial protection, each vial should be completed within 4 hours of piercing the rubber stopper.



Infusion rates - adults

Intragam® 10	Privigen® 10%	Flebogamma® 5%	Flebogamma® 10%	Gamunex® 10%
Adults First 15 minutes: 1 mL/minute Second 15 minutes: Gradually increase rate to a maximum of 3-4 mL/minute. See slide 10 for slower rates for patients at risk or with previous reactions	Initial infusion rate 0.3mL/kg/hr. If well tolerated, gradually increase rate to 4 .8mL/kg body weight/hr	First 30 minutes: 0.01 – 0.02 mL/kg/min If well tolerated, the rate of administration may be gradually increased to a maximum of 0.10 mL/kg/min	First 30 minutes: 0.01mL/kg/min Second 30 minutes: 0.02mL/kg/min Third 30 minutes: 0.04 mL/kg/min Fourth 30 minutes: 0.06 mL/kg/min Fifth 30 minutes: 0.08 mL/kg/min	First 30 minutes: 0.01mL/kg/min If well tolerated, the rate may be gradually increased to a maximum of 0.08mL/kg/min
Maximum rate = 4mL/min = 240mL/hr	Maximum rate =0.08mL/kg/min =4.8mL/kg/hr	Maximum rate = 0.1mL/kg/min = 6mL/kg/hr	Maximum rate = 0.08mL/kg/min =4.8mL/kg/hr	Maximum rate =0.08mL/kg/min =4.8mL/kg/hr

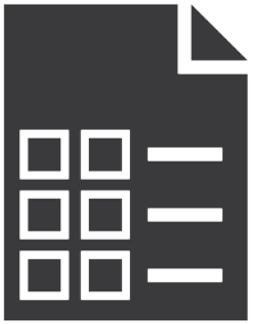
See Slides 10, 12, 14, 16 or 18 for infusion rate calculators

Infusion rates – paediatric/neonatal

- Consideration should be given to running IVIg at slower rates for paediatric/neonatal patients.
- Suggest discussing rate of infusion with a Consultant Paediatrician or Blood Service Haematologist to determine the best rate for each child/infant/neonate.
- Royal Children's Hospital IVIg guideline can be found at:
  - http://www.rch.org.au/bloodtrans/about_blood_products/Intravenous_Immunoglobulin_Guideline/

Infusion rates

- Each product has it’s own individual infusion protocol, **make sure you are using the correct one**
- Infusion via pump is recommended for accuracy
- Start with the smallest vials first, when the infusion rate is slowest as this helps to prevent waste if a reaction occurs



Precautions for all IVIg products

- Consider using a slower maximum rate of infusion for paediatric and neonatal patients, the elderly, those at risk of thrombosis and those with renal insufficiency (check product information)

- Patients should be well hydrated and observed closely during infusion to reduce the risk of adverse events

Patient observation

- Document observations as per hospital policy (minimum suggested vital signs are pre commencement, at each rate increase and post completion)

- Patients with signs of reaction, or who have reacted previously, should be observed closely and more frequently and a slower infusion rate used

- Recommended - out patients remain in the infusion centre for 20 minutes (minimum) following infusion

Adverse events

Some of the more common adverse reactions to IVIg are listed below:

- chills
- headache
- fever
- arthralgia
- vomiting
- allergic reactions
- nausea
- low blood pressure
- moderate low back pain

Respond to reactions as per local policy:

For severe reactions the infusion should be stopped, medical staff notified and MET may be needed

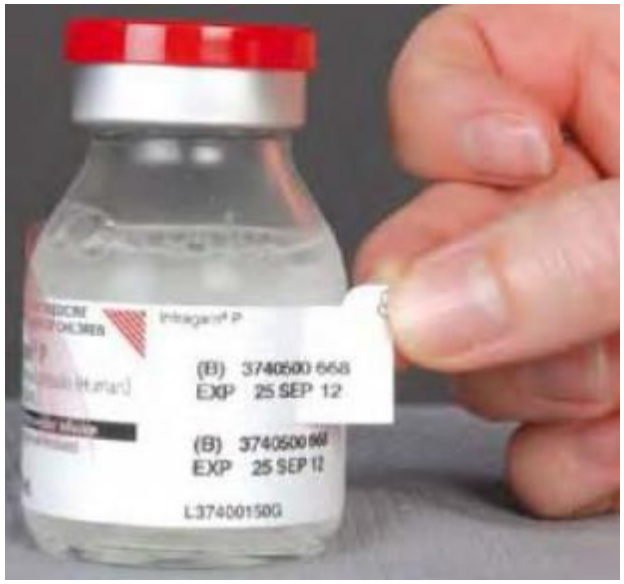
For mild reactions the infusion should be temporarily stopped until the patient improves clinically (5 to 10 minutes)

If the patient improves or on the advice of an MO cautiously recommence at a slower rate

Serious adverse events should be reported to the manufacturer

Traceability

To maintain a link between the product and the recipient always record the product name and batch number in the medical record



Product not used for the intended patient must be returned to the blood bank or pathology provider. It should never be kept in the clinical area for infusion to another patient.

Storage and handling

	Intragam® 10	Privigen® 10%	Flebogamma® 5 & 10%	Gamunex® 10%
Storage	Store at 2-8°C for up to 2 years Once removed from refrigeration, store at room temperature (<25°C) and use within 3 months	Store at room temperature (<25°C) for up to 3 years	Store at room temperature (<30°C) for up to 2 years	Store at 2-8°C for up to 36 months Once removed from refrigeration, store at room temperature (<30°C) and use within 6 months
	Do not freeze Protect from light			
Handling	Do not drop Do not shake			

Subcutaneous immunoglobulin (SCIg)

For patients with suitable conditions, consideration should be given to moving the patient to SCIg.

Why use SCIg?

- Patients can self administer SCIg at home and have greater control of their own care
- Stable immunoglobulin levels, leading to:
  - Fewer infections
  - Less frequent infections
  - Less serious infections
  - Reduced hospital admissions
- Improved compliance with treatment
- Do not need IV access
- Systemic side effects are rare

Further information is available on the Blood Matters website:
https://www2.health.vic.gov.au/hospitals-and-health-services/patient-care/speciality-diagnostics-therapeutics/blood-matters/scig-implementation-program

Useful links

- Victorian Australian Red Cross Blood Service Transfusion Nurses contact: vtatn@redcrossblood.org.au
- Patient information: https://www.blood.gov.au/patient-factsheets-and-resources
- CSL Behring: http://www.csl.com.au/products/product-finder.htm
- Grifols: http://www.grifols.com

References

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