Intravenous immunoglobulin

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

January 2022

VICTORIA State Government

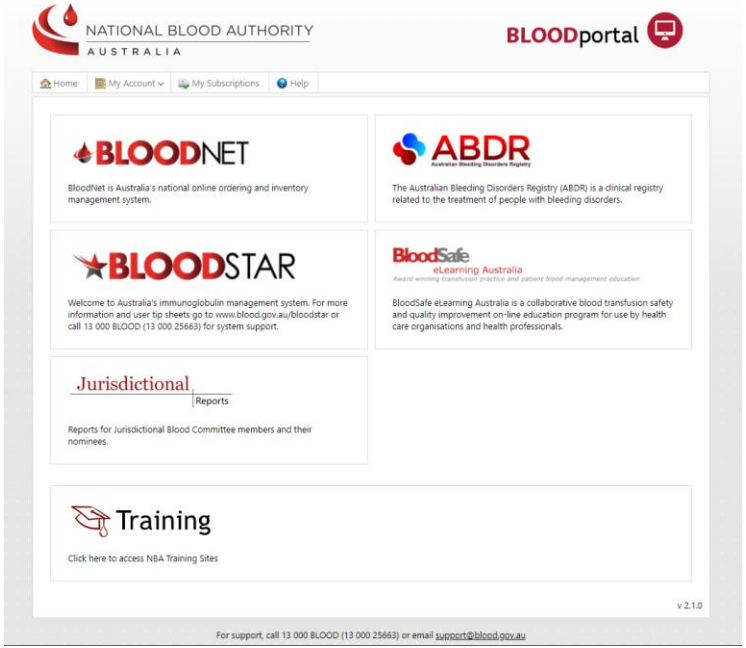
Australian Red Cross Lifeblood

Blood Matters

This presentation is intended to assist with education of clinical staff who provide treatment and care for patients receiving intravenous immunoglobulin therapy.

Background

- Demand for IVIg in Australia continues to grow
- National Blood Authority's initiatives to assist in meeting this demand:
  - Criteria for clinical use – evidence based criteria of conditions for which Ig therapy has ~~proven~~ benefit
  - BloodSTAR – an online system to manage access to the supply of government funded Ig products, based on the Criteria for clinical use
  - Importing product to fill shortfall



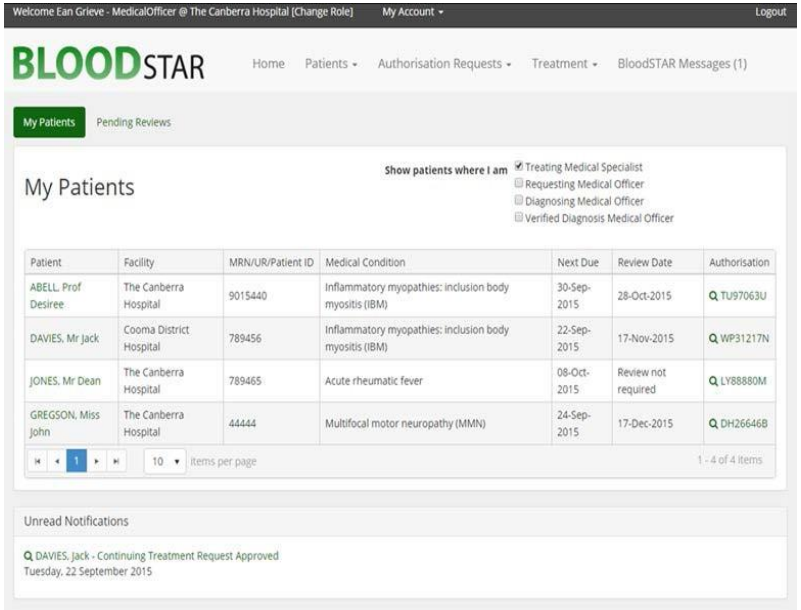
Current supply arrangements

Current supply arrangements		
Domestic IVIg product	Intragam® 10 (10%)	CSL Behring
Imported IVIg products	Flebogamma® 10%	Grifols Australia
	Gamunex® 10%	Grifols Australia
	Privigen® 10%	CSL Behring
	Octagam® 10%	Octapharma
(Start date TBC)	Kiovig® 10%	Takeda
Domestic SCIg product	Evogam® 16%	CSL Behring
Imported SCIg products	Hizentra® 20%	CSL Behring
	Cuvitru® 20%	Takeda
(Start date TBC)	Hyqvia® 10%	Takeda

BloodSTAR

Who uses BloodSTAR?

- **Prescribers** – request authorisation for access to government funded Ig for patient treatment
- **Authorisers** – specified staff of the Australian Red Cross Lifeblood; reviews request and records authorisation outcome in BloodSTAR
- **Nurses/midwives** – confirm patient authorisation status and request Ig from dispenser for individual patient and report adverse events
- **Dispensers** – manage inventory, order products and dispense the correct products to authorised patients and record product transfers



BloodSTAR – view authorisation

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

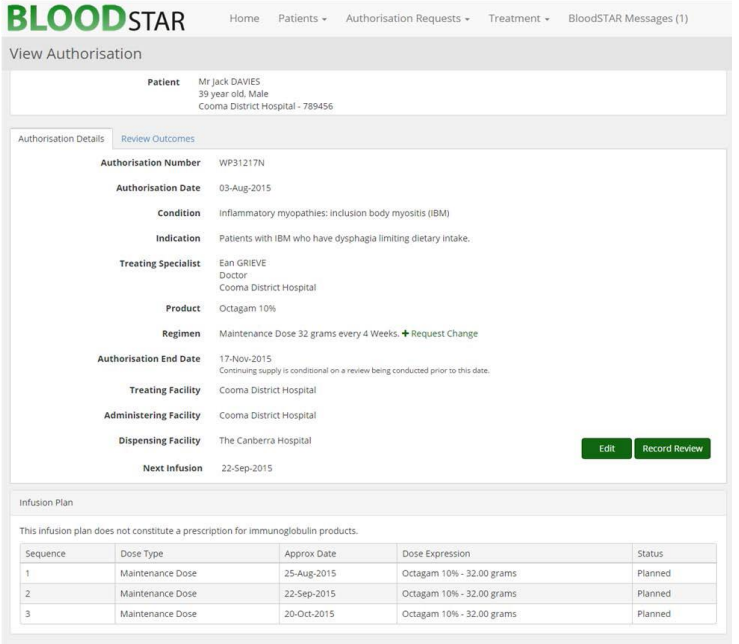
In BloodSTAR:

- Prescribers and nurses/midwives 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

[BloodSTAR-Tip-Sheet-Viewing-authorisation-details-in-BloodSTAR.pdf]



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) Version 3 was released in October 2018

Why did the Criteria change?

- To align with current best-available evidence
- To ensure Ig therapy is available for patients who are likely to benefit from Ig therapy and for whom there are no safe and effective alternative treatments
- To manage the growth in demand for this precious, human-derived product

For more information on the Criteria and the Immunoglobulin Governance program 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

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

Call: 13 000 BLOOD

Jurisdictional direct orders (JDOs)

- Doctors may want to prescribe IVIg for medical conditions that do not meet the Criteria for use
- In this case, the doctor can seek funding for IVIg through local arrangements e.g. local health service therapeutics committee (usually via pharmacy)
- Only imported IVIg is available for purchase under the JDO arrangements for indications that are not listed in the Criteria
- 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	2.5g (25mL), 10g (100mL), 20g (200mL)
Concentration	10%
Source plasma	Australia (volunteer non- remunerated donors)
Stabiliser	Glycine
Storage conditions	• 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.
Infusion rate	• First 15 minutes: 1mL / minute • Thereafter, gradually increase rate to a maximum 3-4mL / minute • Maximum rate: 4ml/minute, (240mL/ hour)

Image: https://intragam10.cslbehring.com.au/sites/default/files/docs/2018-03/INT0023_Intragam%2010_FAQ%20booklet_HR_NoCrop_0.pdf

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%

Discontinuation of Flebogamma 5% DIF – from Tuesday 1 Feb 2022 (inclusive)

Flebogamma® 10% DIF

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 conditions	• Store below 30°C for up to 2 years • Protect from light. • Do not freeze
Infusion rate	• First 30 minutes: 0.01 mL/kg/minute • Second 30 minutes: 0.02 mL/kg/minute • If tolerated increase by a further 0.02 mL/kg/minute each 30 minutes to maximum 0.08 mL/kg/minute • Maximum rate 0.08mL/kg/minute (4.8mL/kg/hour)

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.

Image: https://www.grifols.com/en/product/-/product/spain/flebogamma_10_dif

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%

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.
Infusion rate	• First 30 minutes: 0.01 mL/kg/minute • If well tolerated gradually increase rate to a maximum of 0.08 mL/kg/minute • Maximum rate: 0.08 mL/kg/minute (4.8mL/kg/hour)

Picture published by Grifols Australia

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

Privigin.com

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.
Infusion rate	• Initial infusion rate: 0.3mL/kg/hour • If well tolerated, the rate can gradually increased at 30 minute intervals to maximum rate • Maximum rate: 0.08mL/kg/minute (4.8mL/kg/hour)

Privigen® 10% infusion rate guide

Infusion Rate		Patient's Weight (kg)											
		10	20	30	40	50	60	70	80	90	100	110	120
		Patient's Weight (lb)											
mL/kg/min	mL/kg/h	22	44	66	88	110	132	154	176	198	220	242	264
0.005	0.3	3	6	9	12	15	18	21	24	27	30	33	36
0.010	0.6	6	12	18	24	30	36	42	48	54	60	66	72
0.015	0.9	9	18	27	36	45	54	63	72	81	90	99	108
0.020	1.2	12	24	36	48	60	72	84	96	108	120	132	144
0.025	1.5	15	30	45	60	75	90	105	120	135	150	165	180
0.030	1.8	18	36	54	72	90	108	126	144	162	180	198	216
0.035	2.1	21	42	63	84	105	126	147	168	189	210	231	252
0.040	2.4	24	48	72	96	120	144	168	192	216	240	264	288
0.045	2.7	27	54	81	108	135	162	189	216	243	270	297	324
0.050	3.0	30	60	90	120	150	180	210	240	270	300	330	360
0.055	3.3	33	66	99	132	165	198	231	264	297	330	363	396
0.060	3.6	36	72	108	144	180	216	252	288	324	360	396	432
0.065	3.9	39	78	117	156	195	234	273	312	351	390	429	468
0.070	4.2	42	84	126	168	210	252	294	336	378	420	462	504
0.075	4.5	45	90	135	180	225	270	315	360	405	450	495	540
0.080	4.8	48	96	144	192	240	288	336	384	432	480	528	576

For further information contact CSL Behring

Octagam® 10%

Available from April 2021

Description	Octagam® 10%
Presentation	2g (20mL), 5g in 50mL, 10g in 100mL, 20g in 200mL
Concentration	10%
Source plasma	European and USA remunerated and non-remunerated donors
Stabiliser	Maltose
Storage conditions	Store at 2-8˚C for up to 2 years. Once removed from refrigeration, store below 25°C for a single period and use within 9 months. Do not freeze Protect from light
Infusion rate	• Initial infusion rate: 0.6-1.2mL/kg/hour for 30 minutes • If well tolerated, the rate of administration may gradually be • increased to a maximum of 7.2 mL/kg/hour. • Suggested rate of increase is 0.6mL/kg/hour each 30 minutes • Maximum infusion rate is 7.2mL/kg/hour

National Blood Authority Australia - Annual Report 2010-11

Octagam® 10% infusion rate

Infusion rate mL/kg/hr	Patient weight (kg)											
	10	**20**	**30**	**40**	**50**	**60**	**70**	**80**	**90**	**100**	**110**	**120**
0.6	6	12	18	24	30	36	42	48	54	60	66	72
1.2	12	24	36	48	60	72	84	96	108	120	132	144
1.8	18	36	54	72	90	108	126	144	162	180	198	216
2.4	24	48	72	96	120	144	168	192	216	240	264	288
3.0	30	60	90	120	150	180	210	240	270	300	330	360
3.6	36	72	108	144	180	216	252	288	324	360	396	432
4.2	42	84	126	168	210	252	294	336	378	420	462	504
4.8	48	96	144	192	240	288	336	384	432	480	528	576
5.4	54	108	162	216	270	324	378	432	486	540	594	648
6.0	60	120	180	240	300	360	420	480	540	600	660	720
6.6	66	132	198	264	330	396	462	528	594	660	726	792
7.2	72	144	216	288	360	432	504	576	648	720	794	864

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

Kiovig®

Available 2021 – date TBC

Description	Kiovig®
Presentation	1g in 10mL, 2.5g in 25mL, 5g in 50mL, 10g in 100mL, 20g in 200mL, 30g in 300mL
Concentration	10%
Source plasma	European and USA remunerated and non-remunerated donors
Stabiliser	Glycine
Storage conditions	Do not store above 25°C. Do not freeze Protect from light
Infusion rate	• Initial infusion rate: 0.5 mL/kg/h • If well tolerated gradually increased, by 0.5mL/kg/hour, every 30 minutes to a rate of 5.0 mL/kg/h • Maximum rate 4 mL/kg/hour

Kiovig® infusion rate

Infusion rate	Patient weight											
mL/kg/hr	10	20	30	40	50	60	70	80	90	100	110	120
0.5	5	10	15	20	25	30	35	40	45	50	55	60
1.0	10	20	30	40	50	60	70	80	90	100	110	120
1.5	15	30	45	60	75	90	105	120	135	150	165	180
2.0	20	40	60	80	100	120	140	160	180	200	220	240
2.5	25	50	75	100	125	150	175	200	225	250	275	300
3.0	30	60	90	120	150	180	210	240	270	300	330	360
3.5	35	70	105	140	175	210	245	280	315	350	385	420
4.0	40	80	120	160	200	240	280	320	360	400	440	480

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

Pre-administration

- Ensure correct product for correct patient available, prescription completed, patent IV
- Document baseline observations
- Assess the patient for signs or symptoms that may later be confused with a transfusion reaction
- Hydration – ensure patient is well hydrated as this will help to reduce the risk of some reactions
- Administer any premedication as prescribed
- Check emergency equipment
- Confirm consent has been obtained

Pre-administration (cont.)

- Perform pre-administration patient and product identification checks (check local policy)
- Have product specific administration guideline available for reference
- Consider timing of administration
- Check all equipment available
- 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.

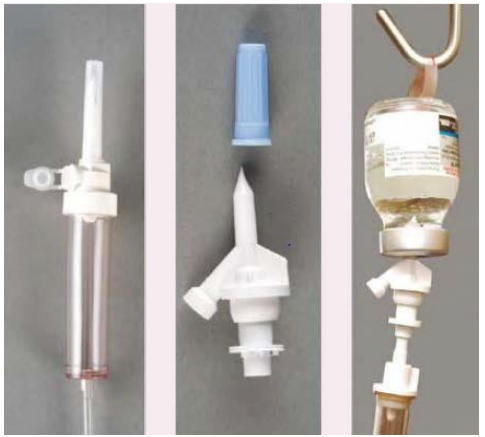


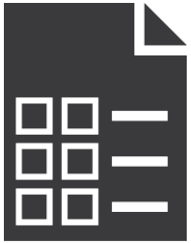
Image: Flippin Blood 2nd edition, 2012

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 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 - adult

- 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:
  - the elderly
  - those at risk of thrombosis
  - those with renal insufficiency
  - paediatric and neonatal patients
    - (check product information and previous slide)

- 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
- 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 according to local policy following infusion

Patient information

Patients should be made aware of:

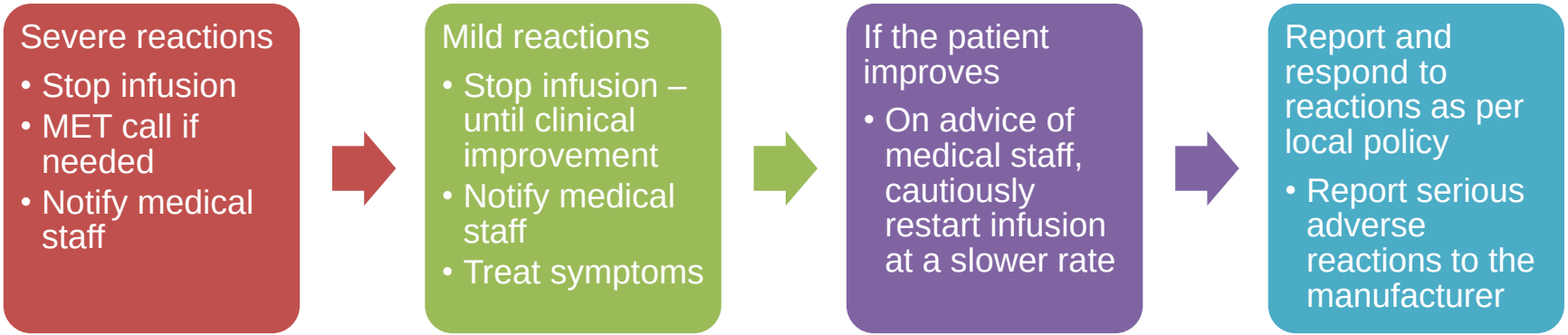
- The potential for delayed side effects of Ig therapy that could occur outside the health care environment. This should include who to contact and when to call an ambulance.
- A clinical expert should discuss with the patient the timing of any vaccines in relation to Ig therapy. Passively acquired antibody, from Ig therapy, can interfere with the response to live, attenuated vaccines.

Adverse events

Some of the more common signs and symptoms for adverse reactions to IVIg

chills headache fever arthralgia	nausea/vomiting rash/allergy	low blood pressure moderate low back pain

Adverse event response



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, pathology provider, pharmacy. It should never be kept in the clinical area for infusion to another patient.

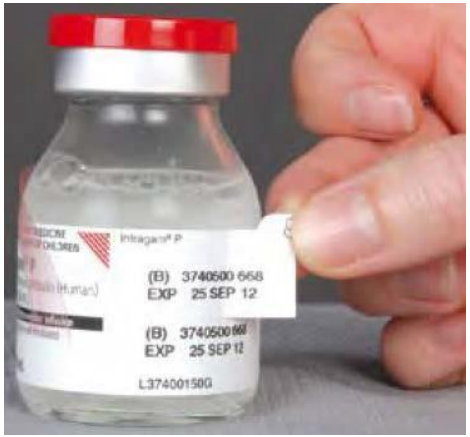


Image: Flippin Blood 2nd edition, 2012

Subcutaneous immunoglobulin (SCIg)

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

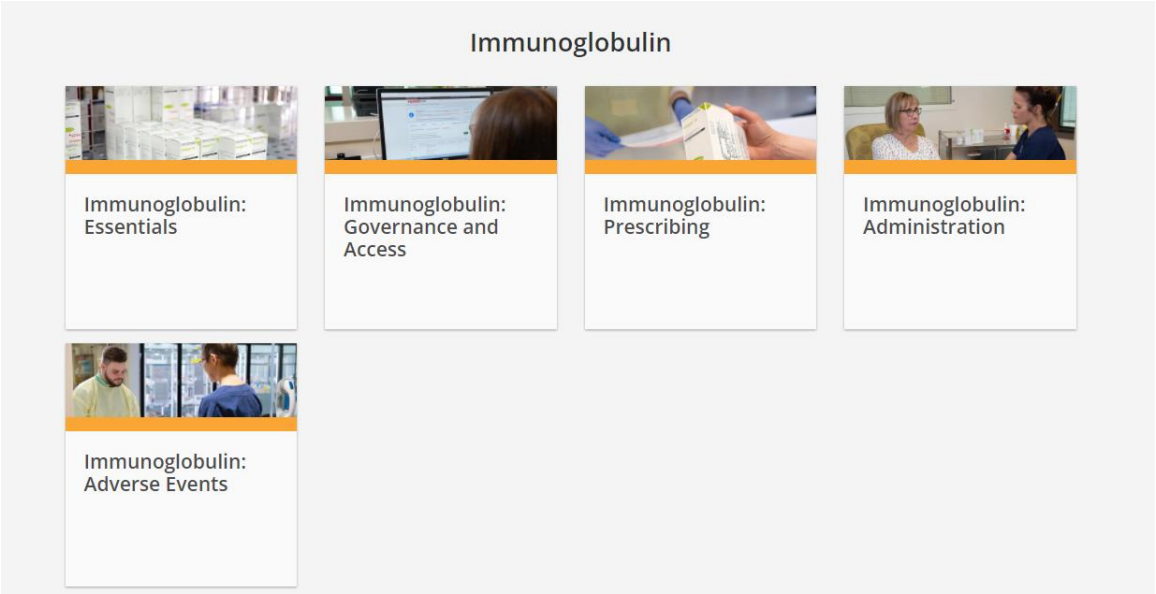
Why use SCIg?

- SCIg can be administered to the patient at home, either self administered or by a carer
- SCIg provides stable immunoglobulin levels, leading to:
  - Fewer or less frequent infections
  - Less serious infections
  - Reduced hospital admissions
- Improved compliance with treatment as the patient has greater control of their own care
- 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/immunoglobulin-replacement-therapy/scig-implementation-program

Further education

BloodSafe® eLearning Australia has a suite of immunoglobulin therapy courses, found at: [BloodSafe eLearning Australia (bloodsafelearning.org.au)]



Useful links

- Victorian Australian Red Cross Lifeblood 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
- Octaphama: https://www.octapharma.com/australia/
- Takeda Pharmaceuticals Australia Pty Ltd. https://www.takeda.com/en-au/what-we-do/our-products/

References

- Flebogamma® 5% DIF, Product Information. Grifols Australia Pty Ltd. 2012 https://www.grifols.com/en/products-services/-/product-search/australia
- Flebogamma® 10% DIF, Product Information. Grifols Australia Pty Ltd. 2013 https://www.grifols.com/en/products-services/-/product-search/australia
- Intragam® 10, Product Information. CSL Behring (Australia) Pty Ltd. 2020 https://www.cslbehring.com.au/products/products-list
- Privigen ®, Product Information. CSL Behring (Australia) Pty Ltd. 2019 https://www.cslbehring.com.au/products/products-list
- Gamunex® 10% Product Information. Grifols Australia Pty Ltd. 2019 https://www.grifols.com/en/products-services/-/product-search/australia
- Octagam® 10% https://www.octapharma.com/australia/
- Kiovig®. Takeda Pharmaceuticals Pty Ltd. 2020 https://www.takeda.com/en-au/what-we-do/our-products/

Acknowledgements

- Australian Red Cross Lifeblood
- Australian governments fund the Australian Red Cross Lifeblood to provide blood, blood products and services to the Australian community.

Accessibility statement and publisher information

To receive this presentation in another format email Blood Matters <Bloodmatters@redcrossblood.org.au>.

Authorised and published by the Victorian Government, 1 Treasury Place, Melbourne.

Available at Blood Matters Program <https://www2.health.vic.gov.au/hospitals-and-health-services/patient-care/speciality-diagnostics-therapeutics/blood-matters>