Subcutaneous immunoglobulin (SCIg) ‘Getting started’

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Australian Red Cross Lifeblood
VICTORIA State Government

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Background

Subcutaneous Immunoglobulin

- Immunoglobulins (also known as antibodies), are glycoprotein molecules produced by plasma cells (white blood cells). They act as a critical part of the immune response by specifically recognizing and binding to particular antigens, such as bacteria or viruses, and aiding in their destruction.
  - Normal IgG level 7 – 12 g/L (these may vary slightly between laboratories)
- The main immunoglobulin in SCIg is IgG (approx 98%)
- Human immunoglobulins have been used to treat hypo-gammaglobulinaemia since the 1950s
- SCIg has been used since the 1980s, but with limited acceptance
- SCIg now widely used in USA, Europe and the UK
- Licenced by NBA in Australia in 2013
- Victorian government funding offer in February 2017 to 12 health services

Facts and figures - Victorian

- 12 health services offered seed funding (February 2017)
- 11 health services have accepted the offer
- 22 health services are now approved SCIg treatment centres
- 17 health services have established a program

- 2181 Victorian patients eligible for SCIg by medical diagnosis
- How many patients are eligible for SCIg by diagnosis (currently receiving IVIg) at the health service?
  - Primary immunodeficiency (PID)?
  - Acquired hypogammaglobulinaemia?
  - Chronic inflammatory demyelinating polyneuropathy (CIDP)?

**Based on BloodSTAR data (Q1 2020-2021)*

Comparison

SCIg	IVIg
You can have it at home	Therapy is usually in a hospital
You give yourself the infusion into the fatty tissue under the skin	An intravenous infusion given by a health care professional
Must meet the SCIg criteria Can be used in patients who have frequent reactions to IVIg	Must meet IVIg criteria
Can be given at a time that fits into your routine, more flexibility and independence Fewer hospital visits, less expensive You must comply with the treatment plan	You are required to attend hospital every month or as required by your doctor [(set routine?) This may be arranged by the hospital at inconvenient times]
Must learn to put in a small needle, draw up the product, use the pump, document event	Report any reactions to the nurse
Approximately 1 hour per infusion 1–2 per week	2–5 hours per infusion 1 per month (4 weeks) or as required by your doctor
More even immunoglobulin levels; may mean fewer infections No 'wear off' effect Local side effects: site swelling, redness and itching at injection site – these can last 1–2 days	Rapid rise in immunoglobulin levels can cause side effects that last for a few days after the infusion Immunoglobulin levels taper off before your next therapy, when you maybe more likely to get an infection You may feel a 'wear off' effect, starting up to a week before your next treatment, when the immunoglobulin levels become low again
Can take SCIg when travelling	Can be difficult sometimes (unworkable) to arrange treatment when you travel

Pros and cons

ASCIA Position Statement - Subcutaneous Immunoglobulin (SCIg)

Table 1: Comparison of Pros and Cons of IVIg and SCIg therapy

	Pros	Cons
IVIg	• Less frequent infusion (monthly) • Rapid increase in serum IgG • Does not require patient training	• Usually hospital based • IV access required • Risk of immediate and systemic adverse effects • Adverse effects from high IgG levels in 12-48 hours post infusion • Symptoms related to wear off effects of IgG trough levels
SCIg	• Home based therapy • IV access not needed • Few systemic side effects • Can be used for patients with previous systemic reactions to IVIg or IV access difficulties - SCIg therapy may be the preferred treatment in these patients • Faster infusion duration • More consistent IgG levels with no wearing off effects related to IgG trough levels • Improved QOL of patient and family with flexibility, independence and empowerment • Reduced hospital costs • Reduced patient travel time and associated costs and inconveniences (e.g. time off school/ work, parking costs). • Patient can take treatment with them when travelling (e.g. on holiday)	• Frequent administration (1-3 times per week) • Local side effects (swelling, induration, local inflammation, itch), which are usually mild and transient • Some patients may require battery or spring driven pumps, although some patients may use the rapid push method which does not require a pump. • Requires treatment plan compliance

https://www.allergy.org.au/images/stories/pospapers/ASCIA_HP_Position_Statement_SCIg_2017.pdf

Source: Adapted from APIIEG

Australasian Society of Clinical Immunology and Allergy (ASCIA) SCIg Position Statement

- SCIg treatment for immunodeficiency is efficacious, well tolerated, has a favourable safety profile and should be available to all patients where clinically appropriate, with relevant education and follow up care.

- Studies have demonstrated:
  - Immune Replacement Therapy using SCIg has equivalent efficacy to IVIg in preventing bacterial infections in patients with antibody deficiencies.
  - Results suggest that maintaining higher steady state IgG levels results in fewer infections.
  - Incidence of infection is inversely related to the steady state IgG level and maintaining higher IgG levels are beneficial, although no given level is necessarily adequate for all patients.
  - Studies indicate that SCIg infusions result in more stable serum immunoglobulin concentrations with little fluctuation in IgG levels compared to the peaks and troughs of IgG levels associated with monthly IVIg administration.
  - More stable IgG levels reduce the risk of immediate and systemic adverse effects due to high IgG levels post-infusion and symptoms related to wearing off effects of IgG trough levels.
- SCIg therapy has been shown to be well tolerated with a low risk of systemic side effects.

- Whilst local tissue reactions are frequent with SCIg therapy, they are often mild and tend to improve over time. Provision of adrenaline autoinjectors is not considered to be necessary, given the demonstrated safety of SCIg infusions.

Based on Recommendation 4 ASCIA Position statement - subcutaneous immunoglobulin (SCIg)
https://www.allergy.org.au/images/stories/pospapers/ASCIA_HP_Position_Statement_SCIg_2017.pdf

Why use SCIg?

- Patients have greater control of their own care
- Stable immunoglobulin levels
- Fewer infections
- Less frequent infections
- Less serious infections
- Reduced hospital admissions
- Improved compliance with treatment
- Do not need IV access
- System side effects are fare

What do the patients want?

- Improved outcomes reported on health related quality of life (HRQoL) scores in patients with PID

  (Home therapy with subcutaneous immunoglobulins for patients with primary immunodeficiency diseases; Elle Haddad et. al. Transfusion and Apheresis Science, 46 (2012) 315 – 321)

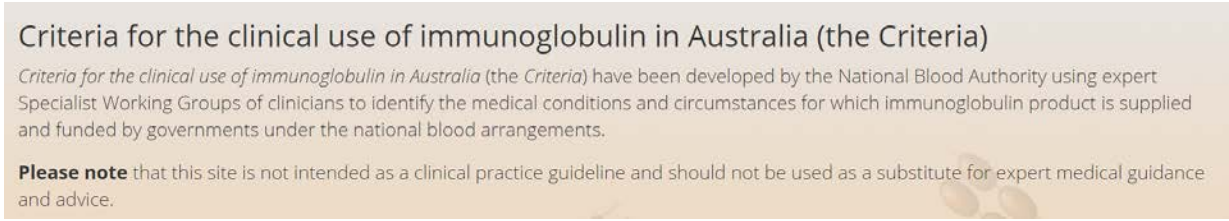
- Most patients prefer SCIg and studies in PID patients have reported improved HRQoL when switching from IVIg to SCIg therapy. (T.M.Windegger et al. / Transfusion Medicine Reviews 31 (2017) 45–50)

- Similar result found for patients with SID although very few studies found (T.M.Windegger et al. / Transfusion Medicine Reviews 31 (2017) 45–50)

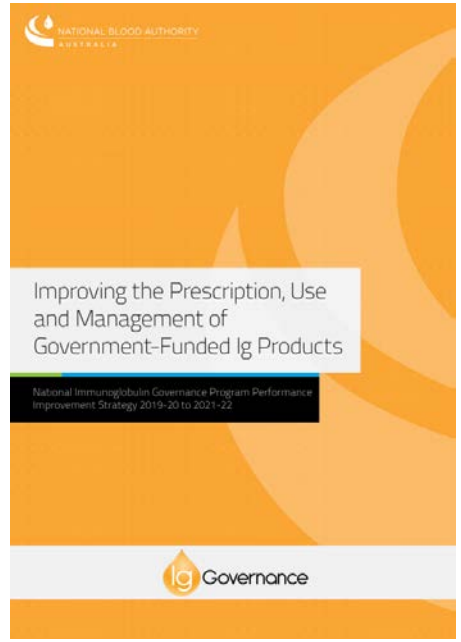
- AusPIPs – [Primary immunodeficiency support group] are engaged and a number using SCIg

Patient eligibility/criteria

- Primary immunodeficiency diseases with antibody deficiency
- Specific antibody deficiency
- Acquired hypogammaglobulinaemia secondary to haematological malignancies:
  - Lymphocytic leukaemia
  - Multiple myeloma
  - Non-Hodgkin lymphoma
  - Other relevant malignancies and post-haemopoietic stem cell transplantation
- Secondary hypogammaglobulinaemia (including iatrogenic immunodeficiency)
- Chronic inflammatory demyelinating polyneuropathy (CIDP)



https://www.criteria.blood.gov.au/



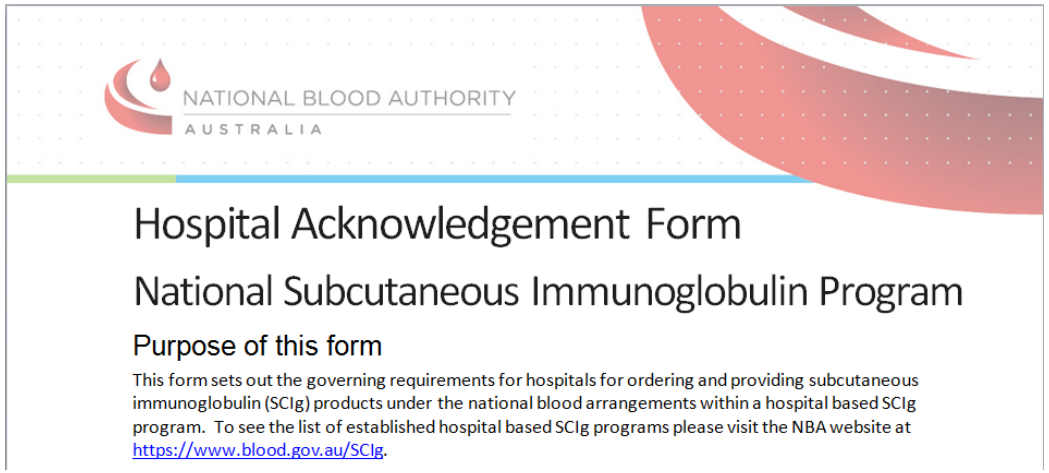
Eligibility criteria

- The patient must be being treated by a clinical specialist within a hospital based SCIg program, where the hospital provides access to all resources and takes full accountability for the management and use of the SCIg product, at no additional cost to patients, and
- Following a patient-specific SCIg request submitted to, and authorised by, the Australian Red Cross Lifeblood (Lifeblood)

Similar to IVIg

Health service eligibility criteria

- The health service must be approved to treat patients with SCIg. A senior clinician needs to complete the Hospital Acknowledgement Form National Subcutaneous Immunoglobulin Program [Requires acknowledgement of by the Chief Executive or Director of Clinical Services (or equivalent)]


NATIONAL BLOOD AUTHORITY
AUSTRALIA

Hospital Acknowledgement Form

National Subcutaneous Immunoglobulin Program

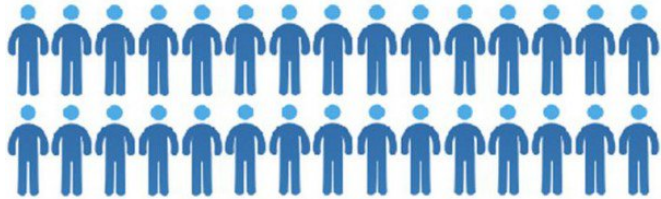
Purpose of this form

This form sets out the governing requirements for hospitals for ordering and providing subcutaneous immunoglobulin (SCIg) products under the national blood arrangements within a hospital based SCIg program. To see the list of established hospital based SCIg programs please visit the NBA website at https://www.blood.gov.au/SCIg.

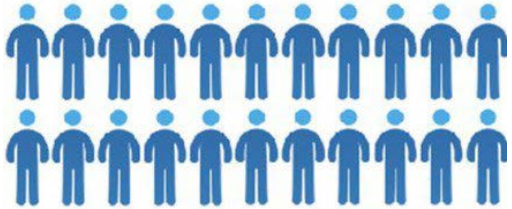
- The completed form must be returned to the to the National Blood Authority - Email: iggovernance@blood.gov.au
  Fax: (02) 6151 5235 (Attention: Ig Governance)

Do you have the numbers?

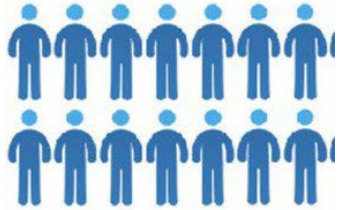
- Baseline data – How many patients do you have that would fit the eligibility criteria?



- How many patients are interested in SCIg treatment?



- How many are suitable for SCIg treatment?



What do you need to start a SCIg program?

- The health service needs to be a SCIg approved treatment centre

  The NBA - Hospital Acknowledgement Form National Subcutaneous Immunoglobulin Program includes governance requirements of the program. https://www.blood.gov.au/system/files/documents/SCIg-hospital-acknowledgment-form-2017-17Oct17.pdf

  Governance:

  - Quality Assurance
  - Equipment and facilities
  - Regular review
  - Reporting unused, discarded, spoilt/broken product
  - Clinical oversight
  - Education and training
  - Supply of product

Governance

Quality Assurance

- *Policies and procedures that provide quality assurance and monitor compliance for the management and use of SCIg in line with the National Safety and Quality Health Service (NSQHS) Standards, particularly Clinical Governance Standard (1) and the Blood Management Standard (7).*
  - Who will write the policies/procedures?
  - Who will monitor compliance?

Clinical oversight

- *A recognised treatment program for the management and use of immunoglobulin for the relevant indications, including an appropriate supervising specialist*
- *Must provide ongoing clinical oversight and support for participating patients*
- *The responsible clinician must consider patient suitability for the self-management and administration of SCIg to ensure appropriate management and use of SCIg product*

Governance

Equipment and facilities

- *Must ensure that patients have access to all necessary equipment and consumables to administer the product,* ***at no additional cost to patients***
  - What equipment will be used?
  - Where will the patient education take place?
  - Where will the patient get the necessary consumables from?
  - Who will ensure the patient has everything they need?

Education and training

- *Must provide education and training for staff and patients*
  - Who will provide the staff education?
  - Checklist for patient education – who will be responsible?
  - Will education be one on one or can it be a group session?

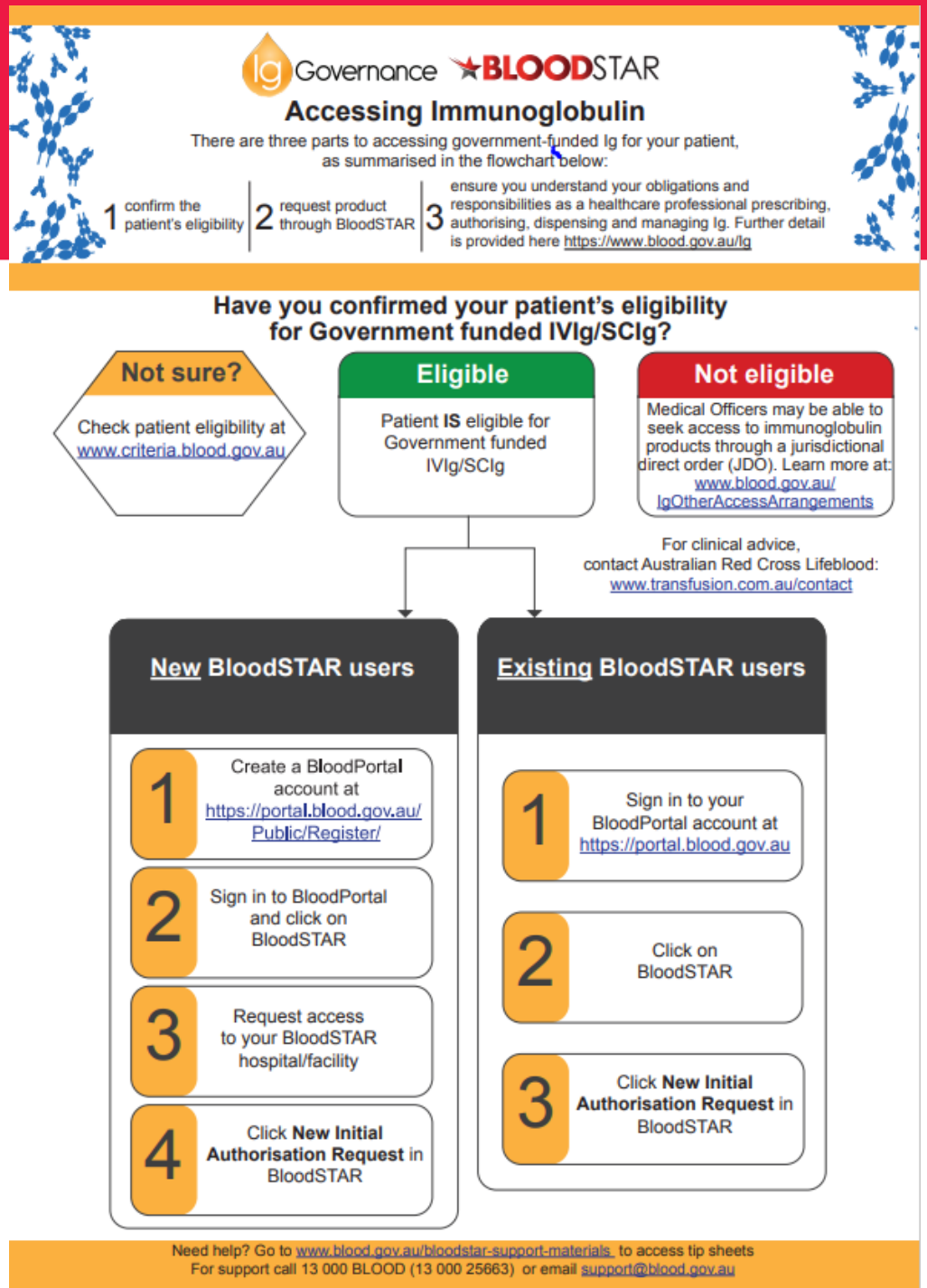
Governance

Regular review

- *To assess clinical benefit of treatment for ongoing therapy should be conducted at periods specified by the responsible clinician in line with the Criteria for Use*
- *Patients should be encouraged to maintain a diary to record SCIg product use and any adverse reactions, as well as collection and management of product as an aid for the clinician at the assessment*
  - Frequency and scheduling of the review; documentation needed – how will you do this?

Accessing SCIg

https://www.blood.gov.au/system/files/My%20patient%20requires%20IVIg-SCIg_V9d.pdf



Governance

Supply of product

- *Orders for SCIg for authorised patients must be managed via BloodSTAR, or alternative arrangements if necessary.*
- *The amount of SCIg supplied to a patient should not exceed more than is required for treatment for two months*
- *Supply and dispensing of SCIg product to patients must be in accordance with relevant state/territory legal requirements*
  - SCIg is an S4 medication and must be dispensed by a pharmacist
  - Requires a medication prescription; must provide a copy to the pharmacy
  - BloodSTAR and BloodNET for traceability

Governance

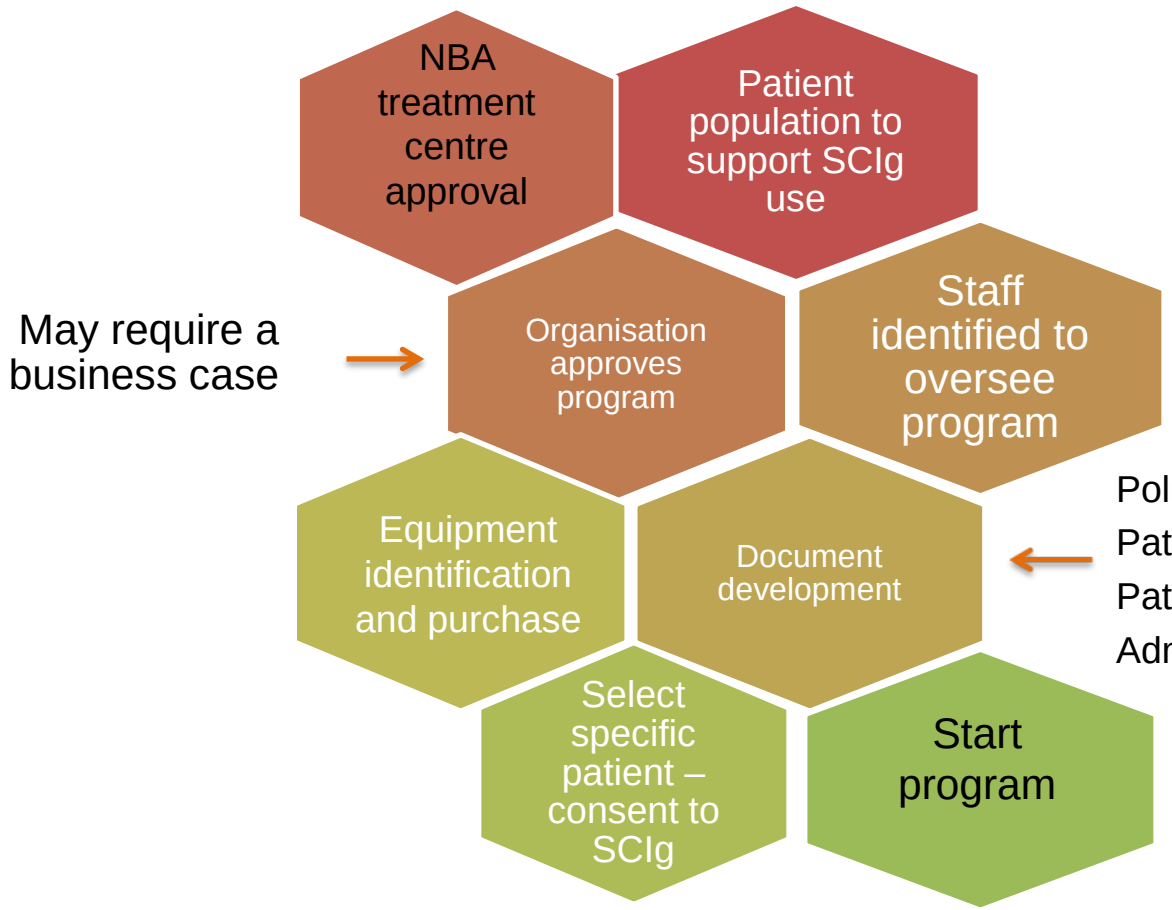
Reporting unused, discarded, spoilt/broken product

- *Patients supplied with SCIg will be expected to report details of unused, discarded or spoilt/broken product to the hospital, to be reported by the hospital through BloodNet*
  - Who will the patient report this to?

Other considerations

- Cost benefit analysis – business case to support the decision (template available on Blood Matters webpage (https://www2.health.vic.gov.au/about/publications/formsandtemplates/business-case-template-scig-program)
- Clinical engagement – medical, nursing and pharmacy staff
- Space – is there a suitable ward/location for patient education?
- BloodSTAR registration, education

Putting the SCIg pieces together



Patient selection

- Willingness to participate in the program. Patients (and/or carers) must agree to do it
- Patient or carer with the physical and mental ability to use SCIg
- Patients with difficult IV access
- Patients who have significant or frequent reactions to IVIg
- Those who travel a long way to get treatment
- Patients who are time poor for any reason and find it difficult to attend for IVIg
- Patients who may be more compliant with SCIg than IVIg – assess reason for non-compliance

Contraindications to SCIg

- Anaphylactic or severe systemic reactions to immunoglobulin (Ig)
- Extensive skin conditions- psoriasis, eczema
- *Cognitive impairment*
- *Poor manual dexterity, decreased hand grip, tremors, poor eyesight*
- IgA deficiency – discuss with immunologist
- Hizentra® - patients with known hyperprolinemia (Type I or II)
- Evogam® - patients known reactions to glycine
- Cuvitru® and Hyqvia® - patients with severe IgA deficiency
- Hyqvia® - patients with known systemic hypersensitivity to hyaluronidase or Vorhyaluronidase alfa, or known systemic hypersensitivity to any of the excipients

Products and vials

	Hizentra®	**Evogam®**	**Cuvitru®**	**Hyqvia®** Comprised of two vials, Ig and corresponding quantity of Vorhyaluronidase alfa.
Plasma source	Imported	Local	Imported	Imported
Stabilizer	Proline	Glycine	Glycine	Glycine
Concentration	20%	16%	20%	10%
Storage	25° C	2 – 8° C	25° C	2 - 8° C
Vial sizes	• 1g (5mL), 2g (10mL), 4g (20mL), 10g (50mL)	• 0.8g (5mL), 1.6g (10mL), 3.2g (20mL)	• 1g (5mL), 2g (10mL), 4g (20mL), 8g (40mL)	• 2.5g (25mL), 5.0g (50mL), 10.0g (100mL), 20.0g (200mL) or 30.0g (300mL) Available vials sizes TBC
Rate	• Start - 15 mL/hr/site • Maximum - 25mL/hr/site	• Start - 10mL/hr/site • Maximum - 20mL/hr/site	• Individualised based on serum IgG trough levels and clinical response	• Refer to product information
Frequency	• Daily • Weekly • Fortnightly	• Weekly	• Individualised	• Refer to product information

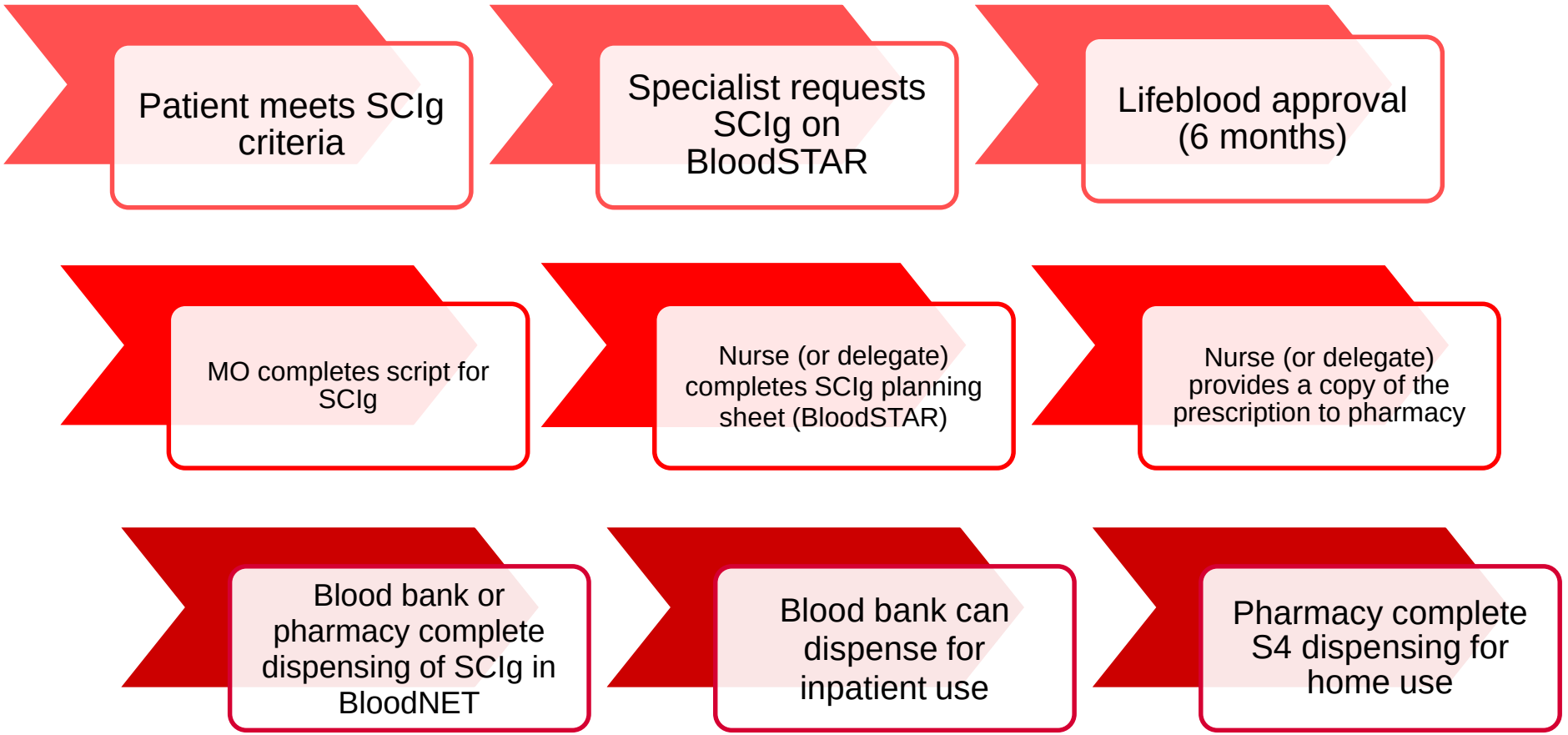
*This information has been summarised using the manufacturer's product information (PI) and has not been subject to manufacturer endorsement. When considering these products, review of the full PI is encouraged .

Ordering

BloodSTAR

- Patient needs to meet criteria for SCIg and MO needs to get authorisation for SCIg
- Nursing (or delegated) staff order the product using a planning sheet in BloodSTAR. *This is how the Blood bank or pharmacy in the health service are notified of the order*
- Blood bank (or pharmacy) order the product from the Lifeblood via BloodNET
- Product is delivered to the Blood bank (or pharmacy)
- For inpatient care, the product can be issued to the ward by Blood bank (or pharmacy)
- For home-care the product needs to be dispensed by pharmacy *(S4 medication)*
- In some cases the product can be ordered by treating facility and delivered to a rural hospital/pharmacy *(by agreement)*
- Need a process to advise the Blood bank/pharmacy what vial sizes are needed for the patient, so the right dose can be given on a weekly basis

Ordering (flow)



Patient education

Education should include:

- Hand washing
- Equipment
- Pumps
- Storage and transport of the product
- Injection site
- Dose and rate calculations (Versarate – when using the EMED system)
- Checking, preparing and drawing up the product
- Priming the line and needle insertion technique
- Adverse reactions and management
- Documentation of the infusion

Equipment

- Cooler (provided by CSL Behring for patients using Hizentra)
- Small band aid or gauze
- Subcutaneous needles and tubing
- Alcohol swabs
- Luer lock syringe(s)
- Drawing up needles
- Surgical tape/dressing
- SCIg product – check dose and expiry
- Infusion pump
- Sharps container
- Infusion Diary/MyHizentra App
- Antibacterial wipes (to clean a work surface; CSL provide a “placemat” for the patients using Hizentra)

Needle sets

	EMED	**HIgH-flo** (can be used with any pump)	**Neria** (can be used with any pump)
Needle gauge	24 & 27	24 & 26	27G
Needle length	6mm, 9mm, 12mm	4mm, 6mm, 9mm, 12mm and 14mm	Steel:8mm and 10mm Soft: 9mm
Tubing	36 inch / 70cm	20 inch; extension set available	80cm for single lumen 90cm for multi lumen 110cm for soft cannula
Needle sets	1, 2, 3, 4 lumens	Sets are available in 1, 2, 3, 4, 5, & 6 configurations. (A Y-connector to combine sets for up to 8 sites)	Steel: 1, 2 or 4 lumens Soft: 1 lumen
Wings	Y	Y	Y
Adhesive	Dressing included	Dressing included	Built-in adhesive dressing

Needle sets

	Butterfly needle Terumo	**BD Saf-T-Intima**
Needle gauge	21, 23, 25	20, 22, 24
Needle length	19mm	19mm
Tubing	30cm, 9cm	Short
Needle sets	1	1
Wings	Y	Y
Adhesive	Dressing not included	Dressing not included

Pumps

Emed - SCIg 60 infusion system

- Spring driven
- 50/60mL BD syringe
- Uses a rate controller – Versarate & Versarate plus

https://www.emedtc.com/products

Springfuser ® syringe infusion pump - 10, 30 or 50

- Spring driven
- 10mL, 30mL or 50mL syringe (pump size indicates syringe size)
- Flow rate control tubing and syringe come as a set (purchased separately)
- Needles purchased from alternate suppliers

Pumps

Niki T34™
- Battery powered
- Programmable – rate control
- Up to 50mL options

FREEDOM60®
- Spring driven
- Uses flow control tubing
- 60mL BD syringe

FreedomEdge®
- Spring driven
- Uses flow control tubing
- 20-30 mL syringe

Documentation

Record in the patient treatment diary (My Hizentra App)/medical record:

- Product name
- Batch number
- Dose
- Volume
- Infusion time
- Infusion site
- Infusion rate
- Symptoms/side effects

Summary

- Stakeholder engagement
- Policy/procedure development
- Staff education and check list
- Patient education and checklist
- Patient review
- Equipment
- Product choice
- Patient selection

Questions to you

- What support/assistance do you need?
- Business case
- Policy/procedure
- Staff education and checklist
- Patient education and checklist
- FAQs

Further information:

Contact: Trechelle Herington

Blood Matters Project Nurse

Phone: 03 9694 0126

Blood Matters SCIg information, tools and resources:

https://www2.health.vic.gov.au/hospitals-and-health-services/patient-care/speciality-diagnostics-therapeutics/blood-matters/immunoglobulin-replacement-therapy/scig-implementation-program

Acknowledgement

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

BloodSTAR

BloodSTAR Support material

https://www.blood.gov.au/bloodstar-support-materials

Two part process

1. Blood portal user registration – create user name and password for all NBA systems
2. BloodSTAR role request – requesting a role and location for access to your facility