Position Statement
Subcutaneous Immunoglobulin (SCIg)

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Introduction

Immunoglobulin replacement therapy (IRT) is used to treat adults and children with primary immune deficiencies (PID)* and other medical conditions, including secondary immune deficiencies (SID), who require immunoglobulin (antibody) replacement.

IRT is administered using intravenous immunoglobulin (IVIg) or subcutaneous immunoglobulin (SCIg) and pharmacokinetics differ according to administration route.

SCIg infusions are administered by slowly injecting purified immunoglobulin (Ig) into fatty tissue underneath the skin. SCIg can be administered at home by patients or carers, using an infusion pump (spring loaded or battery powered) or by rapid push (a manual method that does not require a pump).

This document provides recommendations regarding SCIg therapy in Australia and New Zealand.

* **Inborn errors of immunity (IEI)** include **primary immune deficiencies (PID)** and are a group of more than 550 potentially serious chronic medical conditions. They are caused by defects in genes that control the immune system and can lead to frequent or severe infections, and other chronic immune system disorders, including autoimmune problems.

This Position Statement is not specific for IEI/PID and can be used by other medical specialties.

Key Words

Immunoglobulin (Ig)

Immunoglobulin G (IgG)

Immunoglobulin replacement therapy (IRT)

Inborn errors of immunity (IEI)

Intravenous immunoglobulin (IVIg)

Primary immune deficiency (PID) disease

Quality of life (QOL)

Secondary immune deficiency (SID)

Subcutaneous immunoglobulin (SCIg)

Summary of Recommendations

1. Immunoglobulin replacement therapy (IRT) is the standard of care for patients with antibody deficiency due to a primary immune deficiency (PID) disease or secondary immune deficiency (SID). IRT should be readily available to these patients while under the active care of a clinical immunology/allergy specialist (PID or SID) or other specialist physician (SID).

2. Both intravenous immunoglobulin (IVIg) and subcutaneous immunoglobulin (SCIg) replacement therapy comprise standard of care treatment and should be available for patients in Australia and New Zealand with antibody deficiency due to a primary immune deficiency (PID) disease or secondary immune deficiency (SID).

3. The choice of route (IVIg or SCIg) for IRT will depend on several factors, including patient characteristics, clinical indication, venous access, side effects, rural or remote location, treatment plan compliance and patient choice.

4. When prescribing SCIg or IVIg, it is important to ensure that doses are rounded to the full vial size. Immunoglobulin (Ig) 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.

5. SCIg infusions for IRT are efficacious, well tolerated, have a favourable safety profile and should be available to all patients where clinically appropriate, with relevant education, training and follow up care.

Recommendation 1

IRT is the standard of care for patients with antibody deficiency due to a PID disease or SID. IRT should be readily available to these patients while under the active care of a clinical immunology/allergy specialist (PID or SID) or other specialist physician (SID).

PID and SID can predispose patients to recurrent infections and long term organ damage from chronic infections. One of the most important, effective and commonly used treatments for PID is IRT, to replace immunoglobulins (antibodies) that are insufficient in these patients[1,2,3].

IRT is usually required lifelong in patients with PID to prevent or alleviate infections, and this therapy can be life saving[4].

Access to IRT is guided by clear prescribing criteria to ensure clinically appropriate and economical use of immunoglobulin products.

IRT can be administered by:

- Injecting into the vein (IVIg), usually monthly in hospital; or
- Injecting under the skin (SCIg), usually 1-3 times per week, which can be given at home by the patient or carer.

Recommendation 2

Both IVIg and SCIg used for IRT comprise standard of care treatment and should be available for patients in Australia and New Zealand with antibody deficiency due to PID or SID.

The introduction of IRT has greatly improved health related quality of life (QOL) for patients with PID diseases[5].

Both IVIg and SCIg replacement therapy:

- Offer protection from serious bacterial infections[6].
- Have been shown to have good safety profiles[6].

Recommendation 3

The choice of route (IVIg or SCIg) for IRT will depend on several factors, including patient characteristics, clinical indication, venous access, side effects, rural or remote location, treatment plan compliance and patient choice.

Various factors influence the decision as to whether IVIg or SCIg replacement therapy is the best option for a given patient, including availability of immunoglobulin delivery systems, appropriate products, patient factors, logistic considerations, patient preference and cost[7].

There are advantages and disadvantages for both IVIg and SCIg therapy and the preferred route may vary at different times during a given patient's life[8]. For more details refer to Table 1 on page 4.

Other factors that may affect the choice of route for IRT (IVIg or SCIg) include:

- **Patient satisfaction** - this plays an important role in treatment decisions, particularly as patients with PID diseases require lifelong IRT[5].
- **Availability and resourcing of SCIg infusion pumps and consumables**.
- **Availability of SCIg products** - It is important that once a patient has been successfully established on a product there is ongoing supply of this product. Having multiple SCIg product options is useful for patients who have tolerability problems with one or more products.
- **Other medical conditions** - SCIg therapy may be contraindicated in some patients with severe thrombocytopenia, bleeding disorders or for patients on anticoagulation therapy and may also be problematic for patients with widespread eczema[4].
- **Less frequent infusion procedures may be preferred for some young patients**[4,10] - even though SCIg therapy has been shown to be well tolerated in infants and young children.
- **Limited subcutaneous tissue** - this may limit site options for SCIg infusions[11] although it has been successfully administered to infants.

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

Source: Adapted from APIIEG

Recommendation 4

When prescribing SCIg or IVIg, the treating specialist must ensure that doses are rounded to the full vial size:

- IVIg and SCIg are plasma derived products and are therefore a limited resource.
- Prescribing a dose that uses a part of a vial results in unnecessary wastage.
- Vial sizes vary between different products and this must be considered before prescribing.

Recommendation 5

SCIg infusions for IRT are efficacious, well tolerated, have a favourable safety profile and should be available to all patients where clinically appropriate, with relevant education and follow up care.

Studies have demonstrated that IRT using SCIg has equivalent efficacy to IVIg in preventing bacterial infections in patients with antibody deficiencies[1,5,12].

Results from a pooled analysis of seven studies of four SCIg preparations in patients with PID diseases:

- Suggest that maintaining higher steady state IgG levels results in fewer infections[13].
- Show that the 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[13].

Pharmacokinetic studies indicate that SCIg infusions result in more stable serum Ig concentrations with little fluctuation in IgG levels[5,7,9] compared to the peaks and troughs of IgG levels associated with monthly IVIg administration[14].

More stable IgG levels reduce the risk of:

- Immediate and systemic adverse effects due to high IgG levels post-infusion
- 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[5,10].

Whilst local tissue reactions are frequent with SCIg therapy, they are often mild and tend to improve over time[5,10]. Provision of adrenaline (epinephrine) devices is not considered to be necessary, given the demonstrated safety of SCIg infusions.

There is a range of reasons why patients choose to undergo SCIg therapy, including:

- **Patient choice and satisfaction,** which plays an important role in treatment decisions, as patients with PID diseases require lifelong IgG therapy[5].
- **A preference for patient centred rather than institution centred treatments,** which are likely to enhance independence and self-care capabilities.
- **Poor venous access or a history of severe adverse events following IVIg infusion**[9] - SCIg is universally regarded as the preparation of choice for these patients.
- **Difficulties with IVIg therapy for some patients** as the monthly infusions require repeated venous access and may result in wide variation in serum IgG[9].

SCIg can be administered by:

- Mechanical infusion pumps (spring loaded or battery powered); or
- Rapid push (a manual method that does not require a pump - infusion is pushed by hand through a syringe).

The rapid push method can result in rapid infusions that are safe and well tolerated[14], however the ability to administer SCIg by the push method is dependent on patient characteristics, including strength to manually push the syringe. For more details refer to Table 2 on page 6. Some patients who use a pump can also be trained in the push method in case there is a problem with the pump.

Whilst it is widely accepted that patients should not necessarily have to pay for large expenses (e.g. pumps), the minor costs of consumables can possibly be paid for by some patients, in a similar way

that applies to consumables used in other outpatient based therapy. It is also important that restrictions for provision of SCIg do not discriminate against privately insured patients who are not treated at a public hospital.

Sufficient patient education and training at the initiation of SCIg therapy, and follow up care is essential to ensure patient safety and effective treatment delivery:

- Current operating programs suggest initial education and training (e.g. approximately 4-6 sessions) by a skilled nurse or equivalent is required for each patient commencing SCIg therapy[7,10].
- Patients and their families should be continuously supported and offered regular medical and nursing follow up care[10], for monitoring, advice and clinical assessment, equivalent to current IVIg therapy standards of delivery, which necessitate regular contact with care givers in specialist teams.

Ordering and dispensing of SCIg products should be set up in such a way to:

- Maximise patient convenience, with local delivery of sufficient quantity to patient's home, local pharmacy, local hospital or general practitioner to last at least one month.
- Consider allowing delivery or pick up of more than one month's supply for patients who are on long term IRT and have the capacity to store product (it is important to note that some products can be unrefrigerated for specified periods).
- Ensure effective and non-wasteful usage of a limited and expensive resource.

Table 2. Comparison of Pros and Cons of SCIg infusion methods

	Pros	Cons
Manual: Rapid Push	• Inexpensive (no pump required) • Self-empowerment • Rapid infusion rate (short duration) • Portable and flexible • Can be used when pump fails	• Requires manual strength and dexterity • Manual operation required for the duration of the infusion • Larger bore/gauge needle required for infusing
Mechanical infusion pumps: Spring loaded (e.g. Springfusor, SCIG 60, Freedom 60)	• Relatively inexpensive device • Robust (no electronics) and doesn't require servicing • Doesn't require programming • Lightweight, portable and flexible • Automated	• Relatively expensive consumable costs • Limited control of infusion rate and duration in some devices
Mechanical infusion pumps: Battery powered (e.g. Nikki T 34, T34L)	• Relatively inexpensive consumable costs • Automated • Infusion rate and duration can be controlled • Portable and flexible • Usage and compliance can be monitored	• Relatively expensive device cost • Requires service and careful handling • Requires programming and set up • Batteries require recharging or replacing • Repairs may be challenging for rural or remote patients

Further information

Health Professionals: www.allergy.org.au/hp/papers/immunodeficiency

Patients and Carers: www.allergy.org.au/patients/immunodeficiencies

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