European Nursing Guidelines for Immunoglobulin Administration

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Key points and aims

In this document, the sections on hospital-based therapy are intended for clinicians and patients who are new in the administration of immunoglobulins; we hope to provide these people with support and guidance to:

• Ensure the safe preparation and administration of immunoglobulins

• Ensure that the administration of immunoglobulins is as stress-free as possible for the patients and is given in the shortest, but safest time possible

• Manage the patients’ needs and maximize the benefits of therapy while minimizing the risk of complications

• Develop a partnership between patients and clinicians, and between patients and infusion partners

The sections on home-based therapy are intended to provide guidance and support to nurses that educate and train patients in order to:

• Ensure the safe teaching of immunoglobulin preparation and administration by patients

• Ensure that patients have the “know that, know why, know how” knowledge before starting on home therapy

• Empower patients to self-infuse in a safe and as stress-free way as possible

• Develop a partnership between patients and clinicians, and between patients and infusion partners
Structure of the Guidelines

The guidelines aim to address the practicalities of different immunoglobulin administration modalities. They are not written to be read as a whole. Each chapter is self-standing and covers the recommended procedure for each stage of immunoglobulin administration in a particular clinical context. Each core area is presented in an easy-to-follow table format, which includes:

- Advice on the steps required before the first infusion
- Steps to follow for every subsequent infusion
- A list of equipment required
- A clear description of the infusion process, together with the rationale behind each step to maximize comprehension and assimilation
- A list of references where further information can be obtained

Nurses will select the relevant chapter based on three criteria:

1) Where is the immunoglobulin being administered? In a hospital or at home?
2) Who is the patient? An adult or a child?
3) What is the route of administration of the immunoglobulin? Intravenous or subcutaneous? Pump-assisted or manual?
Background of the European Nursing Guideline Committee

During a round table discussion at the 8th meeting of the International Nursing Group for Immunodeficiencies (INGID), Netherlands, 2008, a need for European guidelines was identified. A group of 10 European expert immunology nurses came together in Amsterdam to discuss aims and write the guidelines.

The first meeting took place in July 2014, with independent medical writers to record the meeting minutes and structure the document, and was financially sponsored by Baxter. In October 2015, the current document named 'European Nursing Guidelines for Immunoglobulin Administration' was finalised.

Although the guidelines are named European Nursing Guidelines, they can be used by nurses all over the world. They are written to give an overview of the use of human, normal immunoglobulins as replacement therapy or immunomodulatory therapy in both children and adults with primary and secondary immunodeficiencies, or neurology, haematology and dermatology indications. Local guidelines and regulations regarding the administration of immunoglobulins that differ from the advices given here should be followed.

The 'European Nursing Guidelines for Immunoglobulin Administration' is evidence-based as far as possible. At the last page an explanation of different levels of evidence in clinical and medical literature is given.
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## Glossary

<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.9% NaCl solution</td>
<td>Also called normal saline, isotonic saline or physiological saline</td>
</tr>
<tr>
<td>Adverse event</td>
<td>Includes all immunoglobulin-related side effects and local reactions</td>
</tr>
<tr>
<td>BW</td>
<td>Body weight</td>
</tr>
<tr>
<td>CHQ-PF50</td>
<td>Child health questionnaire-Parent form 50, a self-administered questionnaire used to assess parent- (or proxy-) reported health status of their children</td>
</tr>
<tr>
<td>EHIC</td>
<td>European Health Insurance Card</td>
</tr>
<tr>
<td>EMA</td>
<td>European Medical Association</td>
</tr>
<tr>
<td>fSCIG</td>
<td>Facilitated subcutaneous immunoglobulin</td>
</tr>
<tr>
<td>FDA</td>
<td>Food and Drug Administration (US)</td>
</tr>
<tr>
<td>GP</td>
<td>General practitioner</td>
</tr>
<tr>
<td>INGID</td>
<td>International Nursing Group for Immunodeficiencies</td>
</tr>
<tr>
<td>IV</td>
<td>Intravenous</td>
</tr>
<tr>
<td>IVIG</td>
<td>Intravenous immunoglobulin</td>
</tr>
<tr>
<td>LQI</td>
<td>Life quality index, an instrument used to assess treatment satisfaction among patients</td>
</tr>
<tr>
<td>mL</td>
<td>Millilitre</td>
</tr>
<tr>
<td>SC</td>
<td>Subcutaneous</td>
</tr>
<tr>
<td>SCIG</td>
<td>Subcutaneous immunoglobulin</td>
</tr>
<tr>
<td>SF-36</td>
<td>Short Form 36, a multi-purpose, generic, coherent and easily self-administered quality-of-life questionnaire</td>
</tr>
<tr>
<td>Systemic adverse event</td>
<td>Adverse event caused by the presence of IgG in the systemic circulation</td>
</tr>
</tbody>
</table>
Introduction to immunoglobulins

An immunoglobulin or antibody is a Y shaped protein that is produced by plasma cells (from B-cells lymphocytes) and helps to identify and neutralise foreign objects such as bacteria or viruses. These foreign objects are referred to as antigens. Antibodies are formed when the body encounters an antigen and are specifically produced just to fight one type of antigen. You can measure antibodies in the blood after a vaccination to see if the patient has responded to the vaccine. Immunoglobulins also enhance phagocytosis, aid in the neutralization of viruses, and activate the complement system.

Immunoglobulins are extracted from plasma donations. To minimize the risk of transmission of blood borne infections, all donors are tested for some critical blood borne viruses such as hepatitis B and C viruses or HIV. During the plasma fractionation process, independent viral inactivation steps effectively remove or eliminate both enveloped (e.g. hepatitis B and C viruses and HIV) and non-enveloped (e.g. hepatitis A virus and parvo virus B19) viruses. The methods used to prepare immunoglobulin products and to remove viruses vary slightly between companies. A list of products is provided in Appendix 1.

There are several subcutaneous products (16% product to a 20% product) available in Europe, one of them is facilitated immunoglobulin and requires the administration of recombinant human hyaluronidase prior the infusion. There are several IV products available in Europe with concentrations ranging from 5% to 10%. Each product has different levels of IgA and different stabilizers. Research to develop new products is a continuing process.

Replacement therapy

The indications for immunoglobulin therapy vary. Many patients with primary or secondary immunodeficiency are unable to produce (enough) properly working immunoglobulins. Genetic or acquired defects in the cells producing immunoglobulins lead to a failure or a reduction in the amount of antibodies in the blood. Immunoglobulin replacement therapy can help these patients fight infections. There are numerous genetic conditions that can cause primary immunodeficiencies (1), and further information can be found on the INGID webpage (www.INGID.com). Secondary immunodeficiency is caused by damage to the immune system by an extrinsic or environmental factor, such as chemotherapy, monoclonal antibody therapy or bone marrow transplantation, or by severe immunoglobulin loss due to diarrhoea, for example (2).

In replacement therapy, the starting dose is usually 0.4–0.6 mg/kg body weight (BW) per 4 weeks. Some countries administer immunoglobulins at an interval of 3 weeks; please check your local guidelines. There is conflicting evidence that some patients with low immunoglobulin A might have high titres of anti-IgA antibodies that may cause adverse events or non-IgE-mediated anaphylaxis. Therefore, the first infusions (during 4–8 weeks) must always take place in a
hospital setting; this time should also be used for patient education. After that, it is safe to continue the treatment at home (3, 4).

**Immunomodulatory therapy**

Immunomodulatory therapy is used in neurology, haematology and dermatology indications. In Europe, approved indications for immunomodulatory therapy with immunoglobulins are immune-modulated thrombocytopenia, Kawasaki’s disease and Guillain-Barré syndrome. Some of the products are also approved for chronic inflammatory demyelinating polyneuropathy (CIDP) and multi motor neuropathy (MMN). Immunomodulatory therapy is also often used off-label in patients with myasthenia gravis or multiple sclerosis (MS), for example. The starting dose for immunomodulatory therapy is in the range 1.0–3.0 mg/kg BW (5). As doses are significantly higher than in replacement therapy the risk of adverse events is higher. Extra care should be taken with these patients (6, 7).

The choice of administration route, frequency and treatment location for each individual patient needs to be carefully assessed. It should remain flexible during different stages of life and it requires on-going assessment in partnership with the patient.

**References**


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**SCIG and IVIG therapies – a comparison**

**Intravenous and subcutaneous immunoglobulin replacement therapy**
Immunoglobulins are used for the treatment of various diseases and in different indications. Well-established routes of administration are:

- Hospital-based intravenous immunoglobulin therapy (IVIG)
- Home-based IVIG (self-infused or with a home-care nurse)
- Hospital-based subcutaneous immunoglobulin therapy (SCIG)
- Home-based SCIG, daily, weekly or facilitated (every 2–4 weeks) most often self-infused

The decision on the route of administration should consider a number of factors including efficacy, trough level, adverse events, quality of life, patient preference and cost effectiveness.

Study data are available on most of these aspects and in particular for the use of immunoglobulins as replacement therapy. A significant number of studies have enrolled both children and adults. The considerations summarized below are mainly based on a meta-analysis of these studies. This analysis identified all retrospective and prospective cohort studies and randomized, controlled trials comparing IVIG to SCIG from well-known databases without restriction on publication date and language. The meta-analysis included 47 publications and 1,028 evaluable patients (1, 2).

There are fewer data comparing intravenous versus subcutaneous therapy for secondary immunodeficiency and for immunomodulatory therapy, but some considerations also apply to these other indications (3-9).

For replacement therapy, both routes of administration lead to an equally effective prevention of infections (10-15), therefore allowing the consideration of other factors such as adverse events or the individual needs and preferences of the patient. A survey highlighted the demand for different therapy options to meet best the individual needs of the patient population (16, 17). Importantly, either method of administration can be switched at almost any time. This may be indicated because of a change in individual needs of the patient during the course of treatment. Some aspects when considering which treatment administration is the best for the patient are:

**Efficacy**

*No significant preference between the two different routes with regards to infection control*

Several studies have been carried out in antibody deficient paediatric and adult patients to compare the efficacy of IVIG and SCIG defined by the number of infections and days in hospital. Although smaller individual studies have demonstrated trends favouring one over the other route of application (10-14), a meta-analysis did not reveal any significant difference of efficacy between the
two administration methods with respect to prevention of infections (1). Thus, both routes of administration show similar efficacy.

Trough level

*Comparable IgG trough levels in patients receiving SCIG or IVIG replacement therapy*

A number of studies have analysed IgG serum levels achieved by IVIG compared to SCIG administration. In some studies, equivalent doses of immunoglobulins were administered (14, 18-20) while in others the US Food and Drug Administration (FDA) required adjusting in the US for equivalent “areas under the curve” to account for pharmacokinetic differences due to monthly IV and weekly SC administration (10, 13, 19). During the steady state period, most of these studies reported slightly higher trough levels when immunoglobulins were given subcutaneously (10, 13, 14, 18-22). However, a meta-analysis reviewing 31 studies accumulating data from 1059 patients did not find significant differences in serum IgG levels between the two administration routes (1). Nevertheless, SC administration is known to result in a high and stable between-dose serum IgG level (21-23), which may explain the good protection against severe infections. A recent retrospective analysis compared subcutaneous immunoglobulin therapy administered by syringe pump or manual push. The data were collected by reviewing medical records. Mean serum immunoglobulin levels were significantly higher among the patients who used the manual push method compared with pump users (24, 25).

Adverse events

*SCIG administration is associated with lower incidence and severity of adverse events*

As immunoglobulins are proteins derived from the blood of healthy donors, they are themselves immunogenic and therefore have the potential to cause systemic adverse events, which can range from light headache or transient itching to serious non-IgE-mediated anaphylactic reaction. IgE-mediated anaphylaxis is very rare and usually caused by the excipients contained in the products (26). Various studies have compared the risk of adverse events in patients with antibody deficiency receiving IVIG or SCIG therapy (10, 12-14, 20-22, 24, 25, 27-29). Most of these studies found subcutaneous administration to be well-tolerated and only reported mild adverse events locally confined to the infusion site. With IVIG administration – due to the rapid dispersion of immunoglobulins through the whole organism – systemic adverse events tend to be more severe. Therefore, SCIG is a therapeutic alternative for patients with a history of IVIG-related systemic adverse events, including those with anti-IgA antibodies (21). However, patients with serious systemic adverse events with IVIG may also be more prone to local reactions with SCIG (22).

Quality of life

*Clear improvements in quality of life and treatment satisfaction in patients switching from hospital based IVIG to home based SCIG therapy*

Several studies have focused on the question of patient- and parent-reported outcomes of immunoglobulin treatment, e.g. health-related quality of life (11, 12,
European Nursing Guidelines for Immunoglobulin Administration

20, 29-36). Several well-established questionnaires were used to collect quality of life data, the most frequently used being the generic SF-36 (36 items), the Child-health Questionnaire, Parental Form (CHQ-P50, 50 items), and the Life Quality Index (LQI). Patients were asked for input on aspects such as convenience, preference, family activity, independence, flexibility, bodily pain, general feasibility, emotional wellbeing, parental impact, and responsibility for their health. All studies and analyses revealed a clear improvement in quality of life, health perception and treatment satisfaction for patients receiving home-based treatment with SCIG. In addition to more frequent family activities owing to treatment flexibility, fewer days missed at work or school and less bodily pain, patients reported that they felt empowered and responsible for their health. SCIG self-administration at home was easy to learn and considered flexible enough to integrate seamlessly into everyday life. In contrast, patients already on self-infused home-based IVIG therapy, switching to self-infused home-based SCIG therapy on the same dose did not show a significant increase in self-reported health-related quality of life, as they may already be satisfied with their treatment location (33). Interestingly, a significant health improvement health was reported in these patients once they switched from IVIG home-therapy to SCIG home-therapy (32). Some patients also prefer to remain on hospital-based IVIG (37).

Costs (home-based SCIG and hospital-based IVIG)

Economic perspective: home-based SCIG replacement therapy is cheaper than hospital based IVIG replacement therapy

Lifelong immunoglobulin therapy is an expensive treatment. To assess the financial burden for healthcare systems, calculations have been performed to compare the estimated costs of different routes of administration (29, 38-43). Among other factors, a direct comparison of the costs of SCIG versus IVIG therapy needs to consider for example the following variables:

1. Mode of administration (subcutaneous with a syringe driver or as manual push without infusion pump)
2. Hospital versus home based intravenous administration
3. Discount prices for intravenous products and consumables for large-scale consumers (hospital)
4. The need to purchase medical equipment such as infusion pumps for each patient (home-based therapy) versus for many patients (hospital-based therapy)
5. Missed working or school days during hospital based IVIG therapy

In one study, directly comparing different administration routes (home-based IVIG, hospital-based IVIG and home-based SCIG), the most cost-effective route was shown to be home-based IVIG therapy (38). In other studies, home-based SCIG was found to be more cost-effective than hospital or home-based IVIG administration (29, 39-42). A recent study demonstrated that home-based SCIG administration by manual push was more cost-effective than hospital-based IVIG (43). Overall, even though the individual studies are difficult to compare, it appears that the home-based administration route is often the most
cost-effective method for healthcare systems and also reduces costs for patients/families (44).

### ROUTE OF ADMINISTRATION

<table>
<thead>
<tr>
<th>ROUTE OF ADMINISTRATION</th>
<th>Efficacy</th>
<th>Trough level</th>
<th>Adverse events</th>
<th>Quality of life</th>
<th>Costs</th>
<th>Other criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Subcutaneous</strong></td>
<td>• Comparable to IVIG</td>
<td>• Stable serum IgG levels between infusions (often once per week)</td>
<td>• Very low risk of systemic adverse events</td>
<td>• Increase of flexibility and activity</td>
<td>• Higher cost when administered in hospital setting</td>
<td>• No venous access necessary</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Associated with initially high incidence of local reactions (mild and usually subsiding with time)</td>
<td>• Can be performed at home</td>
<td>• Lower cost when delivered as home therapy</td>
<td>• Simple treatment monitoring (trough levels)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Better perception of health and increased responsibility for their own health</td>
<td>• However, associated with a reduction in costs in comparison to hospital or home-IVIG therapy</td>
<td>• Necessity for subcutaneous education and understanding the procedure</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Decrease in the number of days missed from work/school due to therapy</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>• Less bodily pain</td>
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<td></td>
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<td></td>
<td></td>
<td>• Less time required per infusion, but higher frequency of infusions</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>• Monthly administration and larger volumes are possible with facilitated SCIG: a dose of hyaluronidase is administered prior to the immunoglobulin product</td>
<td></td>
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</tr>
<tr>
<td><strong>Intravenous</strong></td>
<td>• Comparable to SCIG</td>
<td>• Plasma IgG levels vary greatly during each treatment cycle: after the peak levels recorded shortly after infusion, plasma IgG levels decrease to reach a trough level right prior to the next infusion.</td>
<td>• Associated with the risk of serious adverse events</td>
<td>• Less frequent administration than with SCIG is usually sufficient</td>
<td>• Higher cost when administered in hospital setting</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• More frequent moderate adverse events (e.g. headache, fever, nausea, back pain)</td>
<td>• Possibility to administer large doses in a relatively short time</td>
<td>• Lower cost when delivered as home therapy</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Home therapy possible in some countries</td>
<td></td>
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</tbody>
</table>

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**15**
Other criteria

- Rapid bioavailability
- Simple treatment monitoring (trough levels)
- Necessity for intravenous education and understanding the procedure
- Regular direct contact with the clinician

References


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review and economic analysis. Canadian Agency for Drugs and Technologies in Health HTA, \textbf{36}, 1-8.


Tips and tricks to ensure compliance among your patients

**Your patient’s preference**
Finding out each patient’s treatment preferences increases compliance and therefore maximizes treatment efficacy and safety. Investigate the following preferences:
- Administration route and equipment (pump for example)
- Treatment location (home or hospital)
- Treatment frequency (from daily to monthly)
- Day and time of treatment (particularly relevant for home-treatment)

**Educate your patient**
Thorough education about the disease, the importance of the prescribed medication, and health-related quality life improvements is crucial for compliance.

**Partnership**
Developing a partnership with your patients to empower them to self-manage their disease. Also, providing the patient with a single point of contact (i.e. one nurse or small group of nurses) to contact for questions and emergencies.

**Great experience**
Doing your best to make the first infusions comfortable encourages your patient for the future. See to minimize any discomfort, build a relationship with your patient by spending time having tea or coffee, for example, and provide any support required.
1. IVIG hospital administration – in adults

Intravenous IgG (IVIG), depending on the indication, is prescribed and given on regular basis at various doses.

IVIG is well tolerated by the majority of patients. However, if it is not tolerated (i.e. the presence of adverse events), patients may be switched to another product (1). The first infusion with a new product should be monitored carefully for adverse events.

Each patient may require an individualized infusion regimen in order to minimise adverse events and to achieve the desired therapeutic response (2). Once a successful regimen has been established, it should be adhered to at every infusion.

Prior to every infusion, a review of the administration route, adverse events observed with previous infusion, premedication and patient treatment satisfaction should be made.

At the hospital, IVIG is usually administered via an IV pump. However, patients who are trained for IVIG home-therapy may be trained to use gravity drip administration sets.

Check in each product’s package insert if a filter is required.

The patient/legal representative(s) should:
- Be aware of the possible adverse events (including delayed and late adverse event)
- Know what to do in case of adverse event
- Have a telephone contact to call for advice

For detailed rationales, please see explanations below the list

Before the first infusion
- Check the patient’s identity and the prescription according to the hospital policy
- Assess patient’s level of understanding of therapy
- It is advisable to have a written informed consent from the patient; please check with your local guidelines
- Describe possible adverse events to the patient or the legal representative, including possible flu-like symptoms after the first 2 to 3 infusions, and record any adverse events
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- Complete pre-treatment blood tests (according to local protocol/agreement) (Rationale 1)
- Check immunoglobulin trough levels regularly in antibody deficient patients (Rationale 2)
- Assess the patient’s general health, including temperature, pulse and blood pressure (for vital signs, please refer to your local guidelines to see when assessment is required) (Rationale 3)

Pre-infusion assessment for the next infusions
- Check the patient’s identity and the prescription according to the hospital policy
- Advise the patient to drink water before, during and after the infusion (Rationale 4)
- Assess the patient’s well-being and do not start an infusion if the patient has an infection, a temperature, or flu-like symptoms (Rationale 3)
- Assess for any weight loss or gain (Rationale 5)
- Assess that the immunoglobulin product ordered is the product prescribed for the patient, check the product name, dose, and expiry date
- Inspect product for clarity and colour (Rationale 6)
- The immunoglobulin should be at room temperature before the infusion (Rationale 7)
- Assess the need for premedication (Rationale 8)
- Assess if pre-treatment blood tests are required

Equipment
- Immunoglobulin product for intravenous use
- Intravenous (IV) infusion pump
  IV infusion set (flush with 0.9% NaCl solution, according to your hospital guidelines and product package insert)
- IV cannula: gauge size 24G (or 22G)
- Disinfectant
- Cannula dressing
- Gauze
- Post-infusion dressing
- Sharps container

Infusion (3)
(Please see troubleshooting in Appendix 6)
- Wash and disinfect your hands and working surface thoroughly (Rationale 9)
- Prime the administration set with immunoglobulin and start infusion (increase the rate to the maximum rate tolerated by each patient or to the maximum rate advised in the product package insert)
  - For the first two infusions, increase the infusion rate slowly as advised in the package insert (Rationale 7)
  - Note that the maximum rate is lower for the first two infusions than for the following ones (Rationale 7)
- Please refer to local guidelines with regard to vital signs before each rate increase
- For the first two IVIG infusions, the patient should be observed continuously
- Check the peripheral infusion site half-hourly for inflammation (tenderness, swelling, redness) and leakage. STOP the infusion if there are any signs of inflammation, extravasation or adverse events (Rationale 7)
- Assess for signs of anaphylaxis and adverse events and act accordingly (Rationale 7)
- On completion of the infusion, you may flush the administration set with 0.9% NaCl solution to ensure that the total dose is administered (please refer to local guidelines) (Rationale 10)
- Post-infusion, observe the patient as per local guidelines
Before patient discharge, remove the cannula and make sure that access site has completely stopped bleeding and that no haematoma is forming

Dispose of all items according to hospital policy

Is IV access difficult? The use of permanent indwelling ports or central venous lines in antibody deficient patients is strongly discouraged due to the risk of infections and/or thrombotic events. If peripheral access is consistently difficult, subcutaneous IgG therapy (SCIG) is a viable option.

Careful documentation of every IVIG infusion should include:

- The patient's current health status, medications and any changes in this status in the period between infusions
- The product name, dose and batch numbers of the products used (Rationale 10)
- Any pre-medications which were given
- Duration of infusion and any rate titrations made
- Any problems experienced by the patient during infusion and what was done to address them
- Patient treatment/infusion satisfaction
- Next appointment

**Rationale 1**
Patients should be tested for exposure to known blood borne pathogens before starting IVIG therapy. Once immunoglobulin therapy has been started, serologic tests may become positive because of the passively transferred antibodies and not be informative of the patient’s infection status. Normally, health centres test for HIV and hepatitis A, B, and C, and measure complete blood count, hepatic transaminases and renal function before initiating immunoglobulin therapy by any route. In hematologic disease, Coombs’ testing should be done prior to IVIG therapy. In immunodeficient patients, serologic tests are frequently not informative because patients are not able to form antibodies specific for these pathogens. A negative serologic test in a patient with immune deficiency does not mean that the patient has not been exposed to the pathogens. PCR tests are used to detect active infection with Epstein-Barr virus, CMV and Hepatitis B.

**Rationale 2**
To monitor the effectiveness of treatment.

**Rationale 3**
To establish what is normal for each patient and detect potential infusion-related abnormalities. During infusion, an alteration of vital signs could indicate an adverse event. If fever is present and/or other signs of an acute infection the infusion may need to be postponed until antibiotic treatment is started and/or fever settles. Infusing when a patient has an acute infection can lead to antigen-antibody reaction by formation of immune complex. This effect is most common on first infusion as the concentration of antigens is highest at that time. It is important not to confound this effect with systemic adverse events, and to educate patients about the difference so that they do not fear future treatment sessions.
Rationale 4
Patients receiving IVIG should be well hydrated prior to the infusion. This is particularly important for patients with risk factors for thrombosis and/or renal complications of IVIG therapy such as pre-existing renal insufficiency, diabetes mellitus, who are greater than 65 years of age, suffer from paraproteinaemia, heart disease, and/or concomitant use of nephrotoxic agents. In patients who are not able to drink, and if their condition permits, additional IV hydration may be considered. Good hydration reduces the risk of adverse events.

Rationale 5
Immunoglobulin therapy depends on patient weight, among other parameters. Any significant change in weight may indicate a need for dose increase or (less likely) reduction. The weight is also important to calculate the infusion rate.

Rationale 6
The liquid should be clear and transparent; if it is cloudy or has deposits, the product should not be used.

Rationale 7
Systemic adverse events are more likely to occur with cold immunoglobulin solutions (fridge temperature), with the first infusion, a fast infusion, a large infusion, a long interval since the prior infusion, a switch to a new product or batch number, or the presence of a current infection (4, 5). The most common immediate reactions are headache, cold sweat, light dizziness, chills, fever, and muscular pain. These are usually mild and occur within an hour of starting an infusion and disappear within 6 hours. Both pharmacologic and non-pharmacologic interventions (supplying blankets or pillows, heating pads and encouraging the use of relaxation techniques) may be indicated.

Rationale 8
Premedication is usually only given if there has been a recent systemic adverse event. Many adverse events can be minimized or prevented by oral premedication, for example with antihistamines, steroidal or non-steroidal anti-inflammatory agents (5).

Rationale 9
Good hygiene is an important aspect in infection prevention.

Rationale 10
Although the risk of transmission of blood-borne infections with currently licensed IVIG products is minimal, it is still present. The dose, brand, batch number, expiration date, and manufacturer of any immune globulin product infused into any patient should be carefully recorded in the medical record, as is done for all blood products. In addition, patients should be trained to keep their own logs of this information, as it is often required by law to have donor-to-recipient traceability.
European Nursing Guidelines for Immunoglobulin Administration

References


2. IVIG hospital administration – in children

Every country and institution may have different regulations regarding immunoglobulin therapy administration. Some of the steps/measures given below may not be necessary. Please follow your local and national guidelines.

Intravenous IgG (IVIG), depending on the indication, is prescribed and given on regular basis at various doses.

IVIG is well tolerated by the majority of patients. However, if it is not tolerated (i.e. in the presence of adverse events), patients may be switched to another product (1). The first infusion with a new product should be monitored carefully for adverse events.

Each patient may require an individualized infusion regimen in order to minimise adverse events and to achieve the desired therapeutic response (2). Once a successful regimen has been established, it should be adhered to at every infusion.

Prior to every infusion, a review of the administration route, adverse events observed with previous infusion, premedication and patient treatment satisfaction should be made.

At the hospital, IVIG is usually administered via an IV pump. However, patients who are trained for IVIG home-therapy may be trained to use gravity drip administration sets.

Check in each product’s package insert if a filter is required.

The patient/legal representative(s) should:
- Be aware of the possible adverse events (including delayed and late adverse event)
- Know what to do in case of adverse event
- Have a telephone contact to call for advice

For detailed rationales, please see explanations below the list.

Before the first infusion
- Check the patient’s identity and the prescription according to the hospital policy
- Assess the understanding of therapy with the child and its legal representative(s)
- It is advisable to have a written informed consent from the child (from 16 years onwards, please refer to national legislation), and/or from their legal representative(s); please check with your local guidelines
**European Nursing Guidelines for Immunoglobulin Administration**

- Describe possible adverse events to the patient or the legal representative, including possible flu-like symptoms after the first 2 to 3 infusions, and record any adverse events
- Complete pre-treatment blood tests (according to local protocol/agreement) (Rationale 1)
- Check immunoglobulin trough levels regularly in antibody deficient patients (Rationale 2)
- Assess the patient’s general health, including temperature, pulse and blood pressure (for vital signs, please refer to your local guidelines to see when assessment is required) (Rationale 3)

**Pre-infusion assessment for the next infusions**
- Check the patient’s identity and the prescription according to the hospital policy
- Advise the patient to drink water before, during and after the infusion (Rationale 4)
- Assess the patient’s well-being and do not start an infusion if the patient has an infection, a temperature, or flu-like symptoms (Rationale 3)
- Assess for any weight loss or gain (Rationale 5)
- Assess that the immunoglobulin product ordered is the product prescribed for the patient, check the product name, dose, and expiry date
- Inspect product for clarity and colour (Rationale 6)
- The immunoglobulin should be at room temperature before the infusion (Rationale 7)
- Assess the need for premedication (Rationale 8)
- Assess if pre-treatment blood tests are required

**Equipment**
- Local anaesthetic cream/spray may be applied to the venous access site
- Immunoglobulin product for intravenous use
- Intravenous (IV) infusion pump
- IV infusion set (flush with 0.9% NaCl solution, according to your hospital guidelines and product package insert)
- IV cannula: gauge size 24G (or 22G)
- Disinfectant
- Cannula dressing
- Gauze
- Post-infusion dressing
- Sharps container

**Infusion (3)**
(Please see troubleshooting in Appendix 6)
- Wash and disinfect your hands and working surface thoroughly (Rational 9)
- Prepare the patient for cannulation using appropriate topical anaesthetics and distraction therapy if needed (4)
- Prime the administration set with immunoglobulin and start infusion (increase the rate to the maximum rate tolerated by each patient or to the maximum rate advised in the product package insert)
  - For the first two infusions, increase the infusion rate slowly as advised in the package insert (Rationale 7)
  - Note that the maximum rate is lower for the first two infusions than for the following ones (Rationale 7)
- Please refer to local guidelines with regard to vital signs before each rate increase
- Do not leave the child unattended during the infusion
- Check the peripheral infusion site half-hourly for inflammation (tenderness, swelling, redness) and leakage. STOP the infusion if there are any signs of inflammation, extravasation or adverse events (Rationale 7)
Assess for signs of anaphylaxis and adverse events and act accordingly (Rationale 7)
On completion of the infusion, you may flush the administration set with 0.9% NaCl solution to ensure that the total dose is administered (please refer to local guidelines) (Rationale 10)
Post-infusion, observe the patient as per local guidelines
Before patient discharge, remove the cannula and make sure that access site has completely stopped bleeding and that no haematoma is forming
Dispose of all items according to hospital policy

Is IV access difficult? The use of permanent indwelling ports or central venous lines in antibody deficient patients is strongly discouraged due to the risk of infections and/or thrombotic events. If peripheral access is consistently difficult, subcutaneous IgG therapy (SCIG) is a viable option.

Careful documentation of every IVIG infusion should include:
- The patient's current health status, medications and any changes in this status in the period between infusions
- The product name, dose and batch numbers of the products used (Rationale 10)
- Any pre-medications which were given
- Duration of infusion and any rate titrations made
- Any problems experienced by the patient during infusion and what was done to address them
- Patient treatment/infusion satisfaction
- Next appointment

Rationale 1
Patients should be tested for exposure to known blood borne pathogens before starting IVIG therapy. Once immunoglobulin therapy has been started, serologic tests may become positive because of the passively transferred antibodies and not be informative of the patient’s infection status. Normally, health centres test for HIV and hepatitis A, B, and C, and measure complete blood count, hepatic transaminases and renal function before initiating immunoglobulin therapy by any route. In hematologic disease, Coombs’ testing should be done prior to IVIG therapy (www.uptodate.com/contents/general-principles-in-the-use-of-immunoglobulin?source=search_result&search=intravenous+immunoglobulin&selectedTitle). In immunodeficient patients, serologic tests are frequently not informative because patients are not able to form antibodies specific for these pathogens. A negative serologic test in a patient with immune deficiency does not mean that the patient has not been exposed to the pathogens. PCR tests are used to detect active infection with Epstein-Barr virus, CMV and Hepatitis B.

Rationale 2
To monitor the effectiveness of treatment.

Rationale 3
To establish what is normal for each patient and detect potential infusion-related abnormalities. During infusion, an alteration of vital signs could indicate an adverse event. If fever is present and/or other signs of an acute infection the infusion may need to be postponed until antibiotic treatment is started and/or fever settles. Infusing when a patient has an acute infection can lead to antigen-antibody reaction by formation of immune complex. This effect is most common
on first infusion as the concentration of antigens is highest at that time. It is important not to confound this effect with systemic adverse events, and to educate patients about the difference so that they do not fear future treatment sessions.

**Rationale 4**
Patients receiving IVIG should be well hydrated prior to the infusion. This is particularly important for patients with risk factors for thrombosis and/or renal complications of IVIG therapy, such as pre-existing renal insufficiency, diabetes mellitus, paraproteinaemia, heart disease, and/or concomitant use of nephrotoxic agents. In patients who are not able to drink, and if their condition permits, additional IV hydration may be considered. Good hydration reduces the risk of adverse events.

**Rationale 5**
Immunoglobulin therapy depends on patient weight, among other parameters. Any significant change in weight may indicate a need for dose increase or (less likely) reduction. The weight is also important to calculate the infusion rate.

**Rationale 6**
The liquid should be clear and transparent; if it is cloudy or has deposits, the product should not be used.

**Rationale 7**
Systemic adverse events are more likely to occur with cold immunoglobulin solutions (fridge temperature), with the first infusion, a fast infusion, a large infusion, a long interval since the prior infusion, a switch to a new product or batch number, or the presence of a current infection (5, 6). The most common immediate reactions are headache, cold sweat, light dizziness, chills, fever, and muscular pain. These are usually mild and occur within an hour of starting an infusion and disappear within 6 hours. Both pharmacologic and non-pharmacologic interventions (supplying blankets or pillows, heating pads and encouraging the use of relaxation techniques) may be indicated.

**Rationale 8**
Premedication is usually only given if there has been a recent systemic adverse event. Many adverse events can be minimized or prevented by oral premedication, for example with antihistamines, steroidal or non-steroidal anti-inflammatory agents (6).

**Rationale 9**
Good hygiene is an important aspect in infection prevention.

**Rationale 10**
Although the risk of transmission of blood-borne infections with currently licensed IVIG products is minimal, it is still present. The dose, brand, batch number, expiration date, and manufacturer of any immune globulin product infused into any patient should be carefully recorded in the medical record, as is done for all blood products. In addition, patients should be trained to keep their
own logs of this information, as it is often required by law to have donor-to-recipient traceability.

References


3. IVIG self-administration at home

This option is not available in every country. Please check your local guidelines to see if patients can be trained to receive intravenous IgG therapy (IVIG) at home.

Every country and institution may have different regulations regarding immunoglobulin therapy administration. Some of the steps/measures given below may not be necessary. Please follow your local and national guidelines.

The suitability of each patient for home therapy needs to be assessed before starting any patient on home therapy. The attending doctor, the nurse and the patient, all have to agree to start the education and training.

IVIG home-therapy is usually offered to adults only.

Plan the education and training sessions in a schedule with the patient; advise them that learning the technique will take several sessions.

The patient/legal representative(s) should:
- Be aware of the possible adverse events (including delayed and late adverse event)
- Know what to do in case of adverse event
- Have a telephone contact to call for advice

Criteria for inclusion in a home therapy program
(Please see competency assessment document in Appendix 2 and refer your patients to Appendix 5 for adverse event management at home)

• Patient motivation is important, some patients may never want to undertake home therapy
• Dexterity, mental capacity and appropriate support should be considered
• Good veins are essential to be able to train a patient for home-based IVIG
• No adverse events should have been observed during the last several infusions at the hospital
• A telephone must be available at the place of infusion
• It is advisable that the family doctor is informed of the home therapy
• It is strongly advised that an infusion partner is present at the time of infusion; the infusion partner must also be educated
• The patient and infusion partner should be assessed on a regular basis to verify their knowledge about their condition, their treatment, potential adverse events, and infusion technique. The patient's compliance with the therapy should also be checked
Knowledge crucial for home therapy
All patients trained for home therapy should have the following knowledge (1):

- “Know-that” knowledge, which relates to the understanding of the disease, such as diagnosis, prognosis and therapy
- “Know-why” knowledge, which relates to understanding how the patient’s behaviour affects their disease, therapy and daily life
- “Know-how” knowledge, which related to the skills needed to infuse safely
**European Nursing Guidelines for Immunoglobulin Administration**

**IVIG self-administration – education and training**

For detailed rationales, please see explanations below the list. **Patients should have received immunoglobulins and the dose should be firmly established before starting the training. Patients should fit the inclusion criteria for home therapy. An infusion partner needs to be educated to recognise symptoms of adverse events during infusion. It is recommended that the patient and the infusion partner complete a written informed consent after finishing the education.**

### Before the first education and training session

- Assess the patient’s level of understanding of disease, treatment, and technique
- Describe possible adverse events, including possible flu-like symptoms after the first 2 to 3 infusions, and assess the patient’s knowledge and understanding
- Complete pre-treatment blood tests (according to local protocol/agreement) (Rationale 1)
- Immunoglobulin trough levels should be checked regularly, and the patient should know why this is done (Rationale 2)

### Pre-infusion assessment

- Teach the patient to assess their well-being, by teaching them not to infuse when they have an infection, flu-like symptoms, or a temperature
- Advise the patient to drink water before, during and after the infusion (Rationale 3)
- The patient has to assess that the immunoglobulin product ordered is the product prescribed, check the product name, dose, and expiry date
- Show the patient how to inspect the product’s clarity and colour (Rationale 4)
- Remind the patient to verify that the product is at room temperature before the infusion (Rationale 5)
- Advise the patient to have at hand any medication prescribed for use in case of adverse events close at hand

### Equipment

- Immunoglobulin product for intravenous use
- Sterile towel
- Tourniquet
- IV infusion set
- Butterfly needle: gauge size 21G to 24G
- Disinfectant
- Adhesive tape
- Blood sampling equipment if indicated
- Adrenaline auto-injector (discontinued as a routine for all patients in the UK and Sweden as a meta-analysis showed that anaphylaxis has not occurred in home therapy, that auto-injection devices are often out of date and that their use can cause more harm than benefits)
- Sharps container

### Infusion – the patient and/or the infusion partner is educated and trained to (2):

- Wash hands, prepare a clean area before infusion, and use aseptic technique (Rationale 6)
- Prepare for cannulation with a butterfly
- Assess their well-being and not to infuse if they have an infection, flu-like symptoms, or a temperature
- When required, complete pre-treatment blood tests and investigations
- Check the prescription and the medication
- Prime the administration set with immunoglobulin
• Calculate the drop rate and adjust the flow set accordingly (20 drops equal 1 mL, confirm with the local administration set)
• Infuse the immunoglobulin according to the prescribed rate, starting slowly and increasing to the maximum prescribed rate as directed
• Assess if the rate can be increased
• Check the peripheral infusion site half-hourly for inflammation (tenderness, swelling, redness) and leakage. STOP the infusion if there are any signs of inflammation, extravasation or adverse events (Rationale 5)
• Contact emergency services in case of severe adverse events, or the local clinician for milder adverse events
• At the end of the infusion, remove the butterfly, make sure that the access site has completely stopped bleeding
• Dispose of used equipment safely, and complete the infusion log

(Please see troubleshooting in Appendix 6)

Careful documentation of every IVIG infusion must include:
• Current health status, medications and any changes in this status in the period between infusions
• The product name, dose, and batch numbers of the products used (Rationale 7)
• Any pre-medications taken
• Duration of infusion and any rate titrations made
• Any problems experienced by the patient during infusion and what was done to address them
• Patient treatment/infusion satisfaction
• The patient should bring their infusion diary to the next appointment with their prescribing clinician

Rationale 1
Patients should be tested for exposure to known blood borne pathogens before starting IVIG therapy. Once immunoglobulin therapy has been started, serologic tests may become positive because of the passively transferred antibodies and not be informative of the patient's infection status. Normally, health centres test for HIV and hepatitis A, B, and C, and measure complete blood count, hepatic transaminases and renal function before initiating immunoglobulin therapy by any route. In hematologic disease, Coombs' testing should be done prior to IVIG therapy (www.uptodate.com/contents/general-principles-in-the-use-of-immunoglobulin?source=search_result&search=intravenous+immunoglobulin&electedTitle). In immunodeficient patients, serologic tests are frequently not informative because patients are not able to form antibodies specific for these pathogens. A negative serologic test in a patient with immune deficiency does not mean that the patient has not been exposed to the pathogens. PCR tests are used to detect active infection with Epstein-Barr virus, CMV and Hepatitis B.

Rationale 2
To monitor the effectiveness of treatment.

Rationale 3
Patients receiving IVIG should be well hydrated prior to the infusion. This is particularly important for patients with risk factors for thrombosis and/or renal complications of IVIG therapy, such as pre-existing renal insufficiency, diabetes mellitus, who are greater than 65 years of age, suffer from paraproteinaemia,
heart disease, and/or concomitant use of nephrotoxic agents. In patients who are not able to drink, and if their condition permits, additional IV hydration may be considered. Good hydration reduces the risk of adverse events.

**Rationale 4**
The liquid should be clear and transparent; if it is cloudy or has deposits, the product should not be used.

**Rationale 5**
Systemic adverse events are more likely to occur with cold immunoglobulin solutions (fridge temperature), with the first infusion, a fast infusion, a large infusion, a long interval since the prior infusion, a switch to a new product or batch number, or the presence of a current infection (3, 4). The most common immediate reactions are headache, cold sweat, light dizziness, chills, fever, and muscular pain. These are usually mild and occur within an hour of starting an infusion and disappear within 6 hours. Both pharmacologic and non-pharmacologic interventions (supplying blankets or pillows, heating pads and encouraging the use of relaxation techniques) may be indicated.

**Rationale 6**
Good hygiene is an important aspect in infection prevention.

**Rationale 7**
Although the risk of transmission of blood-borne infections with currently licensed IVIG products is minimal, it is still present. The dose, brand, batch number, expiration date, and manufacturer of any immune globulin product infused into any patient should be carefully recorded in the medical record, as is done for all blood products. In addition, patients should be trained to keep their own logs of this information, as it is often required by law to have donor-to-recipient traceability.

**References**


4. SCIG hospital administration – in adults

Every country and institution may have different regulations regarding immunoglobulin therapy administration. Some of the steps/measures given below may not be necessary. Please follow your local and national guidelines.

Subcutaneous IgG (SCIG), depending on the indication, is prescribed and given on regular basis at various doses.

SCIG is well tolerated by the majority of patients, but it is important to note that each patient may react differently to different immunoglobulin products. Each patient may also require an individualized infusion regimen in order to minimise adverse events and to achieve the desired therapeutic response (1). SCIG can be given at a frequency varying from daily to once every 3–4 weeks; the latter is only possible with facilitated SCIG (2-4). Once a successful regimen has been established, it should be adhered to at every infusion. Every follow-up visit should include a review of the administration route, premedication and patient treatment satisfaction. A change of route or product may be required; the geographical location of therapy administration may also be changed (hospital or home-therapy).

Local reactions are seen in about 80% of the patients starting with SCIG. The most common reactions are swelling, redness and induration (5). However, these reactions usually subside over time (6). For further information, please refer to the section on adverse event management (Appendix 4).

SCIG can be administered via a pump or manual push (4, 7, 8).

The patient/legal representative(s) should:
- Be aware of the possible adverse events (including delayed and late adverse event)
- Know what to do in case of adverse event
- Have a telephone contact to call for advice

For patients already receiving IgG therapy, administer the first dose approximately one week after the last infusion of their previous treatment. Different possibilities are available to start treatment-naïve patients on SCIG (see FYI box).
European Nursing Guidelines for Immunoglobulin Administration

**FYI**

Treatment-naïve patients can be started on SCIG treatment with a normal weekly dose. Alternatively, IVIG or SCIG loading doses can be given to help reach steady-state levels more quickly. In this case, the entire weekly dose is given every day for 3 to 5 consecutive days.

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**SCIG – pump administration in adults**

For detailed rationales, please see explanations below the list

### Before the first infusion

- Check the patient’s identity and the prescription according to the hospital policy
- Assess patient’s level of understanding of therapy
- It is advisable to have a written informed consent from the patient; please check with your local guidelines
- Describe possible adverse events to the patient or the legal representative, including possible flu-like symptoms after the first 2 to 3 infusions, and record any adverse events
- Complete pre-treatment blood tests (according to local protocol/agreement) (Rationale 1)
- Check immunoglobulin trough levels regularly in antibody deficient patients (Rationale 2)
- Assess the patient’s general health, including temperature, pulse and blood pressure (for vital signs, please refer to your local guidelines to see when assessment is required) (Rationale 3)

### Pre-infusion assessment for the next infusions

- Check the patient’s identity and the prescription according to the hospital policy
- Assess for any weight loss or gain (Rationale 4)
- Assess that the immunoglobulin product ordered is the product prescribed for the patient, check the product name, dose, and expiry date
- Inspect product for clarity and colour (Rationale 5)
- The immunoglobulin should be at room temperature before the infusion (Rationale 6)
- Although rarely needed with SCIG, assess the need for premedication (Rationale 7)
- Assess if pre-treatment blood tests are required
- Assess the subcutaneous tissue before deciding on the volume: in patients with less subcutaneous tissue, 10 to 15 mL per site per hour can be used as initial dose. Doses can be increased weekly by 2 to 5 mL per site per hour until they reach 20 mL per site (UK PIN guidelines 3.01 and Swedish Nursing Guidelines). Some patients will tolerate up to 25 mL per site per hour, some can be increased to 30 mL per site per hour after 6 months (9-12)

### Equipment

- Immunoglobulin product for subcutaneous use. Please note: doses should be rounded to the nearest whole bottle size, to prevent wastage
- SC infusion pump, able to give adequate infusion rate and pressure
- Needles or mini-spikes and syringes for drawing up the immunoglobulin solution
- Infusion set
- Needle for subcutaneous use, 45° to 90° angle, gauge size 24G to 27G, 6–14 mm length
- Disinfectant
- Gauze
- Adhesive tape
- Sharps container
Infusion (13)
(Please see troubleshooting in Appendix 6)
• Wash and disinfect your hands and working surface thoroughly (Rationale 8)
• Use aseptic technique when preparing and administering infusion
• Draw the immunoglobulin product into a syringe
• Prime the SC infusion set with immunoglobulin up to 1 cm before the tip of the needle (Rational 9)
• The suggested site(s) for SCIG infusion are the abdomen and thighs (see figure). If two sites are required, two opposite sides of the body should be used. Avoid bony prominences, or areas that are scarred, inflamed or infected.

Figure: SCIG infusion sites

Green areas show preferred infusion sites; other alternatives are shown in blue.

• Clean infusion sites with alcohol wipes and allow to dry (not standard practice in all countries)
• Create a skin fold and insert the needle for subcutaneous use into the subcutaneous tissue (at an angle of 45° to 90°, depending on the needle)
• When the needle is placed (and connected to the infusion set), gently pull back the plunger of the syringe to see if any blood flows back into the line. Disconnect the syringe from the infusion set to check for blood (not standard practice in all countries). If blood is observed, change infusion set and insert a new needle in another location (Rationale 10)
• Secure the needle with adhesive dressing or use the dressing provided with the needle
• Attach the infusion set to the pump
• At the end of the infusion, remove the needles and dispose of all disposable supplies according to hospital policy
• Check the infusion site for local reactions
• Assess patient for any other adverse events
• Apply post infusion dressing if required
• Assess patient comfort levels and satisfaction
### Careful documentation of every SCIG infusion should include:

- The patient’s current health status, medications and any changes in this status in the period between infusions
- The product name, dose and batch numbers of the products used (Rationale 11)
- Any pre-medications which were given
- Duration of infusion and any rate titrations made
- Any problems experienced by the patient during infusion and what was done to address them
- Patient treatment/infusion satisfaction
- Next appointment

#### Rationale 1
Patients should be tested for exposure to known blood borne pathogens **before** starting SCIG therapy. Once immunoglobulin therapy has been started, serologic tests may become positive because of the passively transferred antibodies and not be informative of the patient's infection status. Normally, health centres test for HIV and hepatitis A, B, and C, and measure complete blood count, hepatic transaminases and renal function before initiating immunoglobulin therapy by any route. In hematologic disease, Coombs' testing should be done prior to SCIG therapy ([www.uptodate.com/contents/general-principles-in-the-use-of-immunoglobulin?source=search_result&search=intravenous+immunoglobulin&electedTitle](www.uptodate.com/contents/general-principles-in-the-use-of-immunoglobulin?source=search_result&search=intravenous+immunoglobulin&electedTitle)). In immunodeficient patients, serologic tests are frequently not informative because patients are not able to form antibodies specific for these pathogens. A negative serologic test in a patient with immune deficiency does not mean that the patient has not been exposed to the pathogens. PCR tests are used to detect active infection with Epstein-Barr virus, CMV and Hepatitis B.

#### Rationale 2
To monitor the effectiveness of treatment.

#### Rationale 3
To establish what is normal for each patient and detect potential infusion-related abnormalities. During infusion, an alteration of vital signs could indicate an adverse event. If fever is present and/or other signs of an acute infection the infusion may need to be postponed until antibiotic treatment is started and/or fever settles. Infusing when a patient has an acute infection can lead to adverse events such as immune complex reactions.

#### Rationale 4
Immunoglobulin therapy depends on patient weight, among other parameters. Any significant change in weight may indicate a need for dose increase or (less likely) reduction. The weight is also important to calculate the infusion rate.

#### Rational 5
The liquid should be clear and transparent; if it is cloudy or has deposits, the product should not be used.
Rationale 6
Systemic adverse events are very rare in SC administration, however, they are more likely to occur with cold immunoglobulin solutions (fridge temperature), with the first infusion, a fast infusion, a large infusion, a long interval since the prior infusion, a switch to a new product or batch number, or the presence of a current infection (14). The most common immediate reactions are headache, cold sweat, light dizziness, chills, fever, and muscular pain. These are usually mild and occur within an hour of starting an infusion and disappear within 6 hours. Both pharmacologic and non-pharmacologic interventions (supplying blankets or pillows, heating pads and encouraging the use of relaxation techniques) may be indicated. Although local reactions are very common with SC administration (local itchiness, swelling and redness) they are deemed normal and are not considered worrisome.

Rationale 7
Premedication is rarely necessary when using SCIG therapy; it is only given if there has been a recent systemic adverse event. Many adverse events can be minimized or prevented by oral premedication, for example with antihistamines, steroidal or non-steroidal anti-inflammatory agents (14).

Rationale 8
Good hygiene is an important aspect in infection prevention.

Rationale 9
When in direct contact with the skin, immunoglobulins can cause local reactions.

Rationale 10
Accidental IgG infusion in a blood vessel increases the risk of systemic adverse events.

Rationale 11
Although the risk of transmission of blood-borne infections with currently licensed SCIG products is minimal, it is still present. The dose, brand, batch number, expiration date, and manufacturer of any immune globulin product infused into any patient should be carefully recorded in the medical record, as is done for all blood products. In addition, patients should be trained to keep their own logs of this information, as it is often required by law to have donor-to-recipient traceability.

SCIG – manual push administration in adults
For detailed rationales, please see explanations below the list

Before the first infusion
- Check the patient’s identity and the prescription according to the hospital policy
- Assess patient’s level of understanding of therapy
- It is advisable to have a written informed consent from the patient; please check with your local guidelines
- Describe possible adverse events to the patient or the legal representative, including possible flu-like symptoms after the first 2 to 3 infusions, and record any adverse events
**Pre-infusion assessment for the next infusions**
- Check the patient's identity and the prescription according to the hospital policy (Rationale 4)
- Assess for any weight loss or gain (Rationale 4)
- Assess that the immunoglobulin product ordered is the product prescribed for the patient, check the product name, dose, and expiry date
- Inspect product for clarity and colour (Rationale 5)
- The immunoglobulin should be at room temperature before the infusion (Rationale 6)
- Although rarely needed with SCIG, assess the need for premedication (Rationale 7)
- Assess if pre-treatment blood tests are required
- Assess the subcutaneous tissue before deciding on the volume: 10–20 mL per site can be administered daily or on alternate days. The volume can be increased by 2 to 5 mL per site on a weekly basis until reaching 20 mL per site (15)

**Equipment**
- Immunoglobulin product for subcutaneous use. Please note: doses should be rounded to the nearest whole bottle size, to prevent wastage
- Needles or mini-spikes and syringes for drawing up the immunoglobulin solution
- Butterfly needle 23G (blue), approx. 45° insertion angle
- Disinfectant
- Gauze
- Adhesive tape
- Sharps container

**Infusion (13)**
(please see troubleshooting in Appendix 6)
- Wash and disinfect your hands and working surface thoroughly (Rationale 8)
- Use aseptic technique when preparing and administering infusion
- Draw the immunoglobulin into a single syringe
- Remove the drawing needle (or mini-spike) from the syringe and replace it with the butterfly needle
- Do not prime the needle with the immunoglobulin solution (Rationale 9)
- The suggested site(s) for SCIG infusion are the abdomen and thighs (see Figure). Avoid bony prominences, or areas that are scarred, inflamed or infected.

**Figure: SCIG infusion sites**
**European Nursing Guidelines for Immunoglobulin Administration**

Green areas show preferred infusion sites; other alternatives are shown in blue.

- Clean infusion sites with alcohol wipes and allow to dry (not standard practice in all countries)
- Create a skin fold and insert needle into the subcutaneous tissue (at an angle of approx. 45°)
- When the needle is placed, gently pull back the plunger of the syringe to see if any blood flows back. If blood is observed, start over in another location with a new needle (Rationale 10)
- Inject the immunoglobulin gently, with a rate of 1–2 mL per minute per site
- At the end of the infusion, remove the needles and dispose of all disposable supplies according to hospital policy
- Check the injection site for local reactions
- Assess patient for any other adverse events
- Apply post injection dressing if required
- Assess patient comfort levels and satisfaction

<table>
<thead>
<tr>
<th>Careful documentation of every SCIG infusion should include:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• The patient's current health status, medications and any changes in this status in the period between infusions</td>
</tr>
<tr>
<td>• The product name, dose and batch numbers of the products used (Rationale 11)</td>
</tr>
<tr>
<td>• Any pre-medications which were given</td>
</tr>
<tr>
<td>• Duration of infusion and any rate titrations made</td>
</tr>
<tr>
<td>• Any problems experienced by the patient during infusion and what was done to address them</td>
</tr>
<tr>
<td>• Patient treatment/infusion satisfaction</td>
</tr>
<tr>
<td>• Next appointment</td>
</tr>
</tbody>
</table>

**Rationale 1**
Patients should be tested for exposure to known blood borne pathogens **before** starting SCIG therapy. Once immunoglobulin therapy has been started, serologic tests may become positive because of the passively transferred antibodies and not be informative of the patient’s infection status. Normally, health centres test for HIV and hepatitis A, B, and C, and measure complete blood count, hepatic
transaminases and renal function before initiating immunoglobulin therapy by any route. In hematologic disease, Coombs’ testing should be done prior to SCIG therapy (www.uptodate.com/contents/general-principles-in-the-use-of-immunoglobulin?source=search_result&search=intravenous+immunoglobulin&s_electedTitle). In immunodeficient patients, serologic tests are frequently not informative because patients are not able to form antibodies specific for these pathogens. A negative serologic test in a patient with immune deficiency does not mean that the patient has not been exposed to the pathogens. PCR tests are used to detect active infection with Epstein-Barr virus, CMV and Hepatitis B.

Rationale 2
To monitor the effectiveness of treatment.

Rationale 3
To establish what is normal for each patient and detect potential infusion-related abnormalities. During infusion, an alteration of vital signs could indicate an adverse event. If fever is present and/or other signs of an acute infection the infusion may need to be postponed until antibiotic treatment is started and/or fever settles. Infusing when a patient has an acute infection can lead to adverse events such as immune complex reactions.

Rationale 4
Immunoglobulin therapy depends on patient weight, among other parameters. Any significant change in weight may indicate a need for dose increase or (less likely) reduction. The weight is also important to calculate the infusion rate.

Rationale 5
The liquid should be clear and transparent; if it is cloudy or has deposits, the product should not be used.

Rationale 6
Systemic adverse events are very rare in SC administration, however, they are more likely to occur with cold immunoglobulin solutions (fridge temperature), with the first infusion, a fast infusion, a large infusion, a long interval since the prior infusion, a switch to a new product or batch number, or the presence of a current infection (14). The most common immediate reactions are headache, cold sweat, light dizziness, chills, fever, and muscular pain. These are usually mild and occur within an hour of starting an infusion and disappear within 6 hours. Both pharmacologic and non-pharmacologic interventions (supplying blankets or pillows, heating pads and encouraging the use of relaxation techniques) may be indicated. Although local reactions are very common with SC administration (local itchiness, swelling and redness) they are deemed normal and are not considered worrisome.

Rationale 7
Premedication is rarely necessary when using SCIG therapy; it is only given if there has been a recent systemic adverse event. Many adverse events can be
minimized or prevented by oral premedication, for example with antihistamines, steroidal or non-steroidal anti-inflammatory agents (14).

**Rationale 8**
Good hygiene is an important aspect in infection prevention.

**Rationale 9**
When in direct contact with the skin, immunoglobulins can cause local reactions.

**Rationale 10**
Accidental IgG infusion in a blood vessel increases the risk of systemic adverse events.

**Rationale 11**
Although the risk of transmission of blood-borne infections with currently licensed SCIG products is minimal, it is still present. The dose, brand, batch number, expiration date, and manufacturer of any immune globulin product infused into any patient should be carefully recorded in the medical record, as is done for all blood products. In addition, patients should be trained to keep their own logs of this information, as it is often required by law to have donor-to-recipient traceability.

**fSCIG – facilitated with human hyaluronidase (for adults only)**
Facilitated subcutaneous IgG therapy (fSCIG) is an administration method in which hyaluronidase is injected before subcutaneous IgG (SCIG) to improve the ability of the subcutaneous tissue to accept the immunoglobulin product (16).

Hyaluronidase increases the permeability of the subcutaneous tissue by temporarily depolymerizing hyaluronan. With this method, larger volumes can be dispersed in the subcutaneous space (up to an entire monthly dose at once) than is usually possible with conventional SCIG.

The effect of hyaluronidase is temporary; it remains localized to the treatment area and is fully reversed within 24 to 48 hours.

**fSCIG** is contraindicated for patients under 18 years of age.

**fSCIG** can be given to pregnant women and breast-feeding mothers: clinical experience suggests no harmful effects on the course of pregnancy, on the foetus, or the neonate. Nevertheless, caution should be applied and **fSCIG** prescribed only if clearly indicated (17).

For patients previously on other IgG treatment, administration of the first **fSCIG** dose should be timed so as to maintain an adequate serum IgG level depending on the time of last infusion and on the original treatment method (subcutaneous or intravenous).
European Nursing Guidelines for Immunoglobulin Administration

f/SCIG needs a dose ramp-up schedule (see Table 1), which should be planned with the patient. The dose and frequency should be increased slowly from a once-a-week dose to a 3- or 4-weekly dose schedule.

Table 1 f/SCIG dose ramp-up schedule (17)

<table>
<thead>
<tr>
<th>Week</th>
<th>Infusion Number</th>
<th>Dose to inject</th>
<th>Example for 30 g/month</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1st infusion</td>
<td>1-week dose</td>
<td>7.5 g</td>
</tr>
<tr>
<td>2</td>
<td>2nd infusion</td>
<td>2-week dose</td>
<td>15 g</td>
</tr>
<tr>
<td>3</td>
<td>No infusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>3rd infusion</td>
<td>3-week dose</td>
<td>22.5 g</td>
</tr>
<tr>
<td>5</td>
<td>No infusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>No infusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>4th infusion (if needed)</td>
<td>4-week dose</td>
<td>30 g</td>
</tr>
</tbody>
</table>

The patient/legal representative(s) should:
- Be aware of the possible adverse events (including delayed and late adverse event)
- Know what to do in case of adverse event
- Have a telephone contact to call for advice

For detailed rationales, please see explanations below the list.

**Before the first infusion**
- Check the patient's identity and the prescription according to the hospital policy
- Assess patient's level of understanding of therapy
- It is advisable to have a written informed consent from the patient; please check with your local guidelines
- Describe possible adverse events to the patient or the legal representative, including possible flu-like symptoms after the first 2 to 3 infusions, and record any adverse events
- Complete pre-treatment blood tests (according to local protocol/agreement) (Rationale 1)
- Check immunoglobulin trough levels regularly in antibody deficient patients (Rationale 2)
- Assess the patient’s general health, including temperature, pulse and blood pressure (for vital signs, please refer to your local guidelines to see when assessment is required) (Rationale 3)

**Pre-infusion assessment for the next infusions**
- Check the patient's identity and the prescription according to the hospital policy
- Assess for any weight loss or gain (Rationale 4)
- Assess that the immunoglobulin product ordered is the product prescribed for the patient, check the product name, dose, and expiry date
- Inspect product for clarity and colour (Rationale 5)
- The immunoglobulin should be at room temperature before the infusion (Rationale 6)
- Although rarely needed with SCIG, assess the need for premedication (Rationale 7)
- Assess if pre-treatment blood tests are required
- Assess the subcutaneous tissue before deciding on the volume; administer up to 600 mL per site for patients weighing 40 kg or more, and up to 300 mL per site for patients of less than 40 kg

**Equipment**
- Immunoglobulin product for f/SCIG (a dual vial unit containing 10% IgG (100 mg/mL) and
160 U/mL human hyaluronidase). Please note: doses should be rounded to the nearest whole bottle size, to prevent wastage

- Infusion pump able to give adequate infusion rate (max. 300 mL per hour) and pressure (≥11.6 psi or 600 mmHg)
- Needles or mini-spikes and syringes for drawing up the hyaluronidase and immunoglobulin solutions
- Infusion set
- Needle for subcutaneous use, gauge size 24G (minimum)
- Disinfectant
- Gauze
- Adhesive tape
- Sharps container

**Infusion**

(Please see troubleshooting in Appendix 6)

- Wash and disinfect your hands and working surface thoroughly (Rational 8)
- Use aseptic technique when preparing and administering infusion
- Draw the immunoglobulin into a syringe
- Prime the SC infusion set with immunoglobulin
- Draw the full content of the hyaluronidase vial into a single syringe
- The suggested site(s) for fSCIG infusion are the abdomen and thighs (see Figure). If two sites are required, the two infusion sites should be on opposite sides of the body. Avoid bony prominences, or areas that are scarred, inflamed or infected.

**Figure: fSCIG preferred infusion sites (17)**

- Clean infusion sites with alcohol wipes and allow to dry (not standard practice in all countries)
- Create a skin fold and insert the needle for subcutaneous use into the subcutaneous tissue (at an angle of approx. 45°)
- When the needle is placed and connected to the infusion set, and before the hyaluronidase is injected, gently pull back the plunger of the syringe to see if any blood flows back into the line. If blood is observed, change infusion set and insert a new needle in another location (Rationale 9)
- Secure the needle with adhesive dressing or use the dressing provided with the needle
- Attach the syringe with the hyaluronidase to the subcutaneous needle set
- Administer the hyaluronidase by hand at an initial rate of approx. 1 to 2 mL per minute per
infusion site and increase as tolerated

- Within 10 minutes after hyaluronidase administration, attach the infusion set, primed with the immunoglobulin product, to the same needle set used for the hyaluronidase and start the pump according to Table 2

<table>
<thead>
<tr>
<th>Immunoglobulin 10% for infusion 1 and infusion 2 in patients &gt; 40 kg (&lt; 40 kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minutes intervals</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>10 m</td>
</tr>
<tr>
<td>20 m</td>
</tr>
<tr>
<td>30 m</td>
</tr>
<tr>
<td>Remainder of infusion</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Immunoglobulin 10% for infusion 3 and infusion 4 in patients &gt; 40 kg (&lt; 40 kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minutes intervals</td>
</tr>
<tr>
<td>0</td>
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<tr>
<td>20 m</td>
</tr>
<tr>
<td>30 m</td>
</tr>
<tr>
<td>Remainder of infusion</td>
</tr>
</tbody>
</table>

- At the end of the infusion, remove the needles and dispose of all disposable supplies according to hospital policy
- Assess patient for any adverse events
- Check the area around the infusion site for any unexplained or unusual swelling
- Instruct the patient not to do active exercise within 24 hours after infusion
- Assess patient comfort levels and satisfaction
- Apply post infusion dressing if required

**Careful documentation of every fSCIG infusion should include:**
- The patient's current health status, medications and any changes in this status in the period between infusions
- The product name, dose and batch numbers of the products used (Rationale 10)
- Any pre-medications which were given
- Duration of infusion and any rate titrations made
- Any problems experienced by the patient during infusion and what was done to address them
- Patient treatment/infusion satisfaction
- Next appointment

**Rationale 1**
Patients should be tested for exposure to known blood borne pathogens before starting fSCIG therapy. Once immunoglobulin therapy has been started, serologic tests may become positive because of the passively transferred antibodies and not be informative of the patient's infection status. Normally, health centres test for HIV and hepatitis A, B, and C, and measure complete blood count, hepatic transaminases and renal function before initiating immunoglobulin therapy by any route. In hematologic disease, Coombs' testing should be done prior to fSCIG therapy (www.uptodate.com/contents/general-principles-in-the-use-of-immunoglobulin?source=search_result&search=intravenous+immunoglobulin&s
In immunodeficient patients, serologic tests are frequently not informative because patients are not able to form antibodies specific for these pathogens. A negative serologic test in a patient with immune deficiency does not mean that the patient has not been exposed to the pathogens. PCR tests are used to detect active infection with Epstein-Barr virus, CMV and Hepatitis B.

**Rationale 2**
To monitor the effectiveness of treatment.

**Rationale 3**
To establish what is normal for each patient and detect potential infusion-related abnormalities. During infusion, an alteration of vital signs could indicate an adverse event. If fever is present and/or other signs of an acute infection the infusion may need to be postponed until antibiotic treatment is started and/or fever settles. Infusing when a patient has an acute infection can lead to adverse events such as immune complex reactions.

**Rationale 4**
Immunoglobulin therapy depends on patient weight, among other parameters. Any significant change in weight may indicate the need for a dose increase or (less likely) reduction. The weight is also important to calculate the infusion rate.

**Rationale 5**
The liquid should be clear and transparent; if it is cloudy or has deposits, the product should not be used.

**Rationale 6**
Systemic adverse events are very rare in SC administration, however, they are more likely to occur with cold immunoglobulin solutions (fridge temperature), with the first infusion, a fast infusion, a large infusion, a long interval since the prior infusion, a switch to a new product or batch number, or the presence of a current infection (14). The most common immediate reactions are headache, cold sweat, light dizziness, chills, fever, and muscular pain. These are usually mild and occur within an hour of starting an infusion and disappear within 6 hours. Both pharmacologic and non-pharmacologic interventions (supplying blankets or pillows, heating pads and encouraging the use of relaxation techniques) may be indicated. Although local reactions are very common with SC administration (local itchiness, swelling and redness) they are deemed normal and are not considered worrisome.

**Rationale 7**
Premedication is rarely necessary when using SCIG therapy; it is only given if there has been a recent systemic adverse event. Many adverse events can be minimized or prevented by oral premedication, for example with antihistamines, steroidal or non-steroidal anti-inflammatory agents (14).

**Rationale 8**
Good hygiene is an important aspect in infection prevention.
Rationale 9
Accidental IgG infusion in a blood vessel increases the risk of systemic adverse events, such as thrombotic events. Accidental hyaluronidase infusion in a blood vessel is not expected to lead to adverse events, as the enzyme is rapidly deactivated in the bloodstream.

Rationale 10
Although the risk of transmission of blood-borne infections with currently licensed immunoglobulin products is minimal, it is still present. The dose, brand, batch number, expiration date, and manufacturer of any immune globulin product infused into any patient should be carefully recorded in the medical record, as is done for all blood products. In addition, patients should be trained to keep their own logs of this information, as it is often required by law to have donor-to-recipient traceability.

References


17 HyQvia, Summary of Product Characteristics.
5. SCIG hospital administration – in children

Every country and institution may have different regulations regarding immunoglobulin therapy administration. Some of the steps/measures given below may not be necessary. Please follow your local and national guidelines.

Subcutaneous IgG (SCIG), depending on the indication, is prescribed and given on regular basis at various doses.

SCIG is well tolerated by the majority of the patients, but it is important to note that each patient may react differently to different immunoglobulin products. Each patient may also require an individualized infusion regimen in order to minimise adverse events and to achieve the desired therapeutic response (1). SCIG can be given at a frequency varying from daily to once every 3–4 weeks; the latter is only possible with facilitated SCIG (2-4). Once a successful regimen has been established, it should be adhered to at every infusion. Every follow-up visit should include a review of the administration route, premedication and patient treatment satisfaction. A change of route or product may be required; the geographic location of therapy administration may also be changed (hospital or home-therapy).

Local reactions are seen in about 80% of the patients starting with SCIG. The most common are swelling, redness and induration (5). However, these reactions usually subside over time (6). For further information, please refer to the section on adverse event management (Appendix 4).

SCIG can be administered via a pump or manual push (4, 7, 8).

The patient/legal representative(s) should:
- Be aware of the possible adverse events (including delayed and late adverse event)
- Know what to do in case of adverse event
- Have a telephone contact to call for advice

For patients already receiving IgG therapy, administer the first dose approximately one week after the last infusion of their previous treatment. Different possibilities are available to start treatment-naïve patients on SCIG (see FYI box).
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FYI
Treatment-naïve patients can be started on SCIG treatment with a normal weekly dose. Alternatively, IVIG or SCIG loading doses can be given to reach steady-state levels more quickly. In this case, the entire weekly dose is given every day for 3 to 5 consecutive days.

SCIG – pump administration in children
For detailed rationales, please see explanations below the list

Before the first infusion
- Check the patient’s identity and the prescription according to the hospital policy
- Assess the understanding of therapy with the child and its legal representative(s)
- It is advisable to have a written informed consent from the child (from 16 years onwards, please refer to national legislation), and/or from their legal representative(s); please check with your local guidelines
- Describe possible adverse events to the patient or the legal representative, including possible flu-like symptoms after the first 2 to 3 infusions, and record any adverse events
- Complete pre-treatment blood tests (according to local protocol/agreement) (Rationale 1)
- Check immunoglobulin trough levels regularly in antibody deficient patients (Rationale 2)
- Assess the patient’s general health, including temperature, pulse and blood pressure (for vital signs, please refer to your local guidelines to see when assessment is required) (Rationale 3)

Pre-infusion assessment for the next infusions
- Check the patient’s identity and the prescription according to the hospital policy
- Assess for any weight loss or gain (Rationale 4)
- Assess that the immunoglobulin product ordered is the product prescribed for the patient, check the product name, dose, and expiry date
- Inspect product for clarity and colour (Rationale 5)
- The immunoglobulin should be at room temperature before the infusion (Rationale 6)
- Although rarely needed with SCIG, assess the need for premedication (Rationale 7)
- Assess if pre-treatment blood tests are required
- After careful assessment of subcutaneous tissue, 5–10 mL per site can be infused over one hour in babies (1–6 months), or 10 mL per site in 40–60 minutes in children older than 6 months. In older children/young people, 10–25 mL can be infused in 40–90 minutes. Volumes of 25 mL and larger may need to be divided into several sites (9)

Equipment
- Local anaesthetic cream/spray or cryogenic spray may be applied to the SC site (10)
- Immunoglobulin product for subcutaneous use. Please note: doses should be rounded to the nearest whole bottle size to prevent wastage
- SC infusion pump, able to give adequate infusion rate and pressure
- Needles or mini-spikes and syringes for drawing up the immunoglobulin solution
- Infusion set
- Needle for subcutaneous use, 45° to 90° angle, gauge size 24G to 27G, 6–14 mm length
- Disinfectant
- Gauze
- Adhesive tape

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• Sharps container

**Infusion (11)**  
(Please see troubleshooting in Appendix 6)  
• Wash and disinfect your hands and working surface thoroughly (Rationale 8)  
• Use aseptic technique when preparing and administering infusion  
• Draw the immunoglobulin into a syringe  
• Prime the SC infusion set with immunoglobulin up to 1 cm before the tip of the needle (Rationale 9)  
• The suggested site(s) for SCIG infusion are the abdomen and thighs (see figure). If two sites are required, two opposite sides of the body should be used. Avoid bony prominences, or areas that are scarred, inflamed or infected.

**Figure: SCIG infusion sites**

- Green areas show preferred infusion sites; other alternatives are shown in blue.

• Clean infusion sites with alcohol wipes and allow to dry (not standard practice in all countries)  
• Create a skin fold and insert needle for subcutaneous use into the subcutaneous tissue in the area that was anesthetized (at an angle of 45° to 90°, depending on the needle)  
• When the infusion needle is placed, gently pull back the plunger of the syringe to see if any blood flows back into the line. Disconnect the syringe from the infusion set to check for blood (not standard practice in all countries). If blood is observed, change infusion set and insert a new needle in another location (Rationale 10)  
• Secure the needle with adhesive dressing or use the dressing provided with the needle  
• Attach the infusion set to the pump  
• Do not leave the child unattended during infusion  
• At the end of the infusion, remove the needles and dispose of all disposable supplies according to hospital policy  
• Check the infusion site for local reactions  
• Assess patient for any other adverse events  
• Apply post infusion dressing if required  
• Assess patient comfort levels and satisfaction

**Careful documentation of every SCIG infusion should include:**
European Nursing Guidelines for Immunoglobulin Administration

Rationale 1
Patients should be tested for exposure to known blood borne pathogens before starting SCIG therapy. Once immunoglobulin therapy has been started, serologic tests may become positive because of the passively transferred antibodies and not be informative of the patient's infection status. Normally, health centres test for HIV and hepatitis A, B, and C, and measure complete blood count, hepatic transaminases and renal function before initiating immunoglobulin therapy by any route. In hematologic disease, Coombs' testing should be done prior to SCIG therapy (www.uptodate.com/contents/general-principles-in-the-use-of-immunoglobulin?source=search_result&search=intravenous+immunoglobulin&selectedTitle). In immunodeficient patients, serologic tests are frequently not informative because patients are not able to form antibodies specific for these pathogens. A negative serologic test in a patient with immune deficiency does not mean that the patient has not been exposed to the pathogens. PCR tests are used to detect active infection with Epstein-Barr virus, CMV and Hepatitis B.

Rationale 2
To monitor the effectiveness of treatment.

Rationale 3
To establish what is normal for each patient and detect potential infusion-related abnormalities. During infusion, an alteration of vital signs could indicate an adverse event. If fever is present and/or other signs of an acute infection the infusion may need to be postponed until antibiotic treatment is started and/or fever settles. Infusing when a patient has an acute infection can lead to adverse events such as immune complex reactions.

Rationale 4
Immunoglobulin therapy depends on patient weight, among other parameters. Any significant change in weight may indicate a need for dose increase or (less likely) reduction. The weight is also important to calculate the infusion rate.

Rational 5
The liquid should be clear and transparent; if it is cloudy or has deposits, the product should not be used.

Rationale 6
Systemic adverse events are very rare in SC administration, however, they are more likely to occur with cold immunoglobulin solutions (fridge temperature).
with the first infusion, a fast infusion, a large infusion, a long interval since the prior infusion, a switch to a new product or batch number, or the presence of a current infection (12). The most common immediate reactions are headache, cold sweat, light dizziness, chills, fever, and muscular pain. These are usually mild and occur within an hour of starting an infusion and disappear within 6 hours. Both pharmacologic and non-pharmacologic interventions (supplying blankets or pillows, heating pads and encouraging the use of relaxation techniques) may be indicated.

Although local reactions are very common with SC administration (local itchiness, swelling and redness) they are deemed normal and are not considered worrisome.

**Rationale 7**
Premedication is rarely necessary when using SCIG therapy; it is only given if there has been a recent systemic adverse event. Many adverse events can be minimized or prevented by oral premedication, for example with antihistamines, steroidal or non-steroidal anti-inflammatory agents (12).

**Rationale 8**
Good hygiene is an important aspect in infection prevention.

**Rationale 9**
When in direct contact with the skin, immunoglobulins can cause local reaction.

**Rationale 10**
Accidental IgG infusion in a blood vessel increases the risk of systemic adverse events.

**Rationale 11**
Although the risk of transmission of blood-borne infections with currently licensed SCIG products is minimal, it is still present. The dose, brand, batch number, expiration date, and manufacturer of any immune globulin product infused into any patient should be carefully recorded in the medical record, as is done for all blood products. In addition, patients should be trained to keep their own logs of this information, as it is often required by law to have donor-to-recipient traceability.

**SCIG – manual push administration in children**
For detailed rationales, please see explanations below the list

<table>
<thead>
<tr>
<th><strong>Before the first infusion</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Check the patient's identity and the prescription according to the hospital policy</td>
</tr>
<tr>
<td>• Assess the understanding of therapy with the child and its legal representative(s)</td>
</tr>
<tr>
<td>• It is advisable to have a written informed consent from the child (from 16 years onwards, please refer to national legislation), and/or from their legal representative(s); please check with your local guidelines</td>
</tr>
<tr>
<td>• Describe possible adverse events to the patient or the legal representative, including possible flu-like symptoms after the first 2 to 3 infusions, and record any adverse events</td>
</tr>
<tr>
<td>• Complete pre-treatment blood tests (according to local protocol/agreement)</td>
</tr>
</tbody>
</table>

(Rationale 1)
**European Nursing Guidelines for Immunoglobulin Administration**

- Check immunoglobulin trough levels regularly in antibody deficient patients (Rationale 2)
- Assess the patient’s general health, including temperature, pulse and blood pressure (for vital signs, please refer to your local guidelines to see when assessment is required) (Rationale 3)

### Pre-infusion assessment for the next infusions
- Check the patient's identity and the prescription according to the hospital policy
- Assess for any weight loss or gain (Rationale 4)
- Assess that the immunoglobulin product ordered is the product prescribed for the patient, check the product name, dose, and expiry date
- Inspect product for clarity and colour (Rationale 5)
- The immunoglobulin should be at room temperature before the infusion (Rationale 6)
- Although rarely needed with SCIG, assess the need for premedication (Rationale 7)
- Assess if pre-treatment blood tests are required
- After careful assessment of subcutaneous tissue 5–10 mL per site can be infused in babies and young children. In older children or children with good subcutaneous tissue, up to 20 mL per site can be infused. In skinny children, the dose may be split over several sites (Rationale 8)

### Equipment
- Local anaesthetic cream/spray or cryogenic spray may be applied to the SC site (Rationale 9)
- Immunoglobulin product for subcutaneous use. Please note: doses should be rounded to the nearest whole bottle size, to prevent wastage
- Needles or mini-spikes and syringes for drawing up the immunoglobulin solution
- Butterfly needle 23G (blue), approx. 45° insertion angle
- Disinfectant
- Gauze
- Adhesive tape
- Sharps container

### Infusion (Rationale 10)
(Please see troubleshooting in Appendix 6)
- Wash and disinfect your hands and working surface thoroughly (Rationale 11)
- Use aseptic technique when preparing and administering infusion
- Draw the immunoglobulin into a single syringe
- Remove the drawing needle (or mini-spike) from the syringe and replace it with the butterfly needle
- Do not prime the needle with the immunoglobulin solution (Rationale 12)
- The suggested site(s) for SCIG infusion are the abdomen and thighs (see Figure). Avoid bony prominences, or areas that are scarred, inflamed or infected.

*Figure: SCIG infusion sites*
Green areas show preferred infusion sites; other alternatives are shown in blue.

- Clean infusion sites with alcohol wipes and allow to dry (not standard practice in all countries)
- Create a skin fold and insert needle for subcutaneous use into the subcutaneous tissue in the area that was anesthetized (at an angle of approx. 45°)
- When the needle is placed, gently pull back the plunger of the syringe to see if any blood flows back. If blood is observed, start over in another location with a new needle (Rationale 10)
- Inject the immunoglobulin gently, with a rate of 1 mL per minute per site
- At the end of the infusion, remove the needles and dispose of all disposable supplies according to hospital policy
- Check the injection site for local reactions
- Assess patient for any other adverse events
- Apply post injection dressing if required
- Assess patient comfort levels and satisfaction

**Careful documentation of every SCIG infusion should include:**
- The patient’s current health status, medications and any changes in this status in the period between infusions
- The product name, dose and batch numbers of the products used (Rationale 11)
- Any pre-medications which were given
- Duration of infusion and any rate titrations made
- Any problems experienced by the patient during infusion and what was done to address them
- Patient treatment/infusion satisfaction
- Next appointment

**Rationale 1**
Patients should be tested for exposure to known blood borne pathogens before starting SCIG therapy. Once immunoglobulin therapy has been started, serologic tests may become positive because of the passively transferred antibodies and not be informative of the patient’s infection status. Normally, health centres test for HIV and hepatitis A, B, and C, and measure complete blood count, hepatic
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transaminases and renal function before initiating immunoglobulin therapy by any route. In hematologic disease, Coombs’ testing should be done prior to SCIG therapy (www.uptodate.com/contents/general-principles-in-the-use-of-immunoglobulin?source=search_result&search=intravenous+immunoglobulin&selectedTitle). In immunodeficient patients, serologic tests are frequently not informative because patients are not able to form antibodies specific for these pathogens. A negative serologic test in a patient with immune deficiency does not mean that the patient has not been exposed to the pathogens. PCR tests are used to detect active infection with Epstein-Barr virus, CMV and Hepatitis B.

**Rationale 2**
To monitor the effectiveness of treatment.

**Rationale 3**
To establish what is normal for each patient and detect potential infusion-related abnormalities. During infusion, an alteration of vital signs could indicate an adverse event. If fever is present and/or other signs of an acute infection the infusion may need to be postponed until antibiotic treatment is started and/or fever settles. Infusing when a patient has an acute infection can lead to adverse events such as immune complex reactions.

**Rationale 4**
Immunoglobulin therapy depends on patient weight, among other parameters. Any significant change in weight may indicate a need for dose increase or (less likely) reduction. The weight is also important to calculate the infusion rate.

**Rationale 5**
The liquid should be clear and transparent; if it is cloudy or has deposits, the product should not be used.

**Rationale 6**
Systemic adverse events are very rare in SC administration, however, they are more likely to occur with cold immunoglobulin solutions (fridge temperature), with the first infusion, a fast infusion, a large infusion, a long interval since the prior infusion, a switch to a new product or batch number, or the presence of a current infection (12). The most common immediate reactions are headache, cold sweat, light dizziness, chills, fever, and muscular pain. These are usually mild and occur within an hour of starting an infusion and disappear within 6 hours. Both pharmacologic and non-pharmacologic interventions (supplying blankets or pillows, heating pads and encouraging the use of relaxation techniques) may be indicated.
Although local reactions are very common with SC administration (local itchiness, swelling and redness) they are deemed normal and are not considered worrisome.

**Rationale 7**
Premedication is rarely necessary when using SCIG therapy; it is only given if there has been a recent systemic adverse event. Many adverse events can be
minimized or prevented by oral premedication, for example with antihistamines, steroidal or non-steroidal anti-inflammatory agents (12).

Rationale 8
Good hygiene is an important aspect in infection prevention.

Rationale 9
When in direct contact with the skin, immunoglobulins can cause local reaction.

Rationale 10
Accidental IgG infusion in a blood vessel increases the risk of systemic adverse events.

Rationale 11
Although the risk of transmission of blood-borne infections with currently licensed SCIG products is minimal, it is still present. The dose, brand, batch number, expiration date, and manufacturer of any immune globulin product infused into any patient should be carefully recorded in the medical record, as is done for all blood products. In addition, patients should be trained to keep their own logs of this information, as it is often required by law to have donor-to-recipient traceability.

References


6. SCIG self-administration at home – in adults

Every country and institution may have different regulations regarding immunoglobulin therapy administration. Some of the steps/measures given below may not be necessary. Please follow your local and national guidelines.

The suitability of each patient for subcutaneous IgG therapy (SCIG) at home needs to be assessed before starting training. The attending doctor, the nurse and the patient, all have to agree to start the training.

Plan the training sessions in a schedule with the patient; advise them that learning the technique might take several sessions.

Criteria for inclusion in a home therapy program
(Please see competency assessment document in Appendix 3 and refer your patients to Appendix 5 for adverse event management at home)

- Patient motivation is important, some patients may never wish to undertake home therapy
- Compliance
- Dexterity, mental capacity and appropriate support should be considered
- A telephone must be available at the place of infusion
- It is advisable that the family doctor is informed of the home therapy
- The patient and infusion partner should be assessed on a regular basis to verify their knowledge about their condition, their treatment, potential adverse events, and infusion technique. The patient’s compliance with the therapy should also be checked

SCIG is well tolerated by the majority of the patients, but it is important to note that each patient may react differently to different immunoglobulin products. Each patient may also require an individualized infusion regimen in order to minimise adverse events and to achieve the desired therapeutic response (1). SCIG can be given at a frequency varying from daily to once every 3–4 weeks (2-4). Once a successful regimen has been established, it should be adhered to at every infusion. Every follow-up visit should include a review of the administration route, premedication and patient treatment satisfaction. A change of route or product may be required; the geographical location of therapy administration may also be changed (hospital or home-therapy).

Local reactions are seen in about 80% of the patients starting with SCIG. The most common are swelling, redness and induration (5). However, these reactions usually subside over time (6). For further information, please refer to the section on adverse event management (Appendix 5).
European Nursing Guidelines for Immunoglobulin Administration

SCIG can be administered via a pump or manual push (4, 7, 8).

<table>
<thead>
<tr>
<th>The patient/legal representative(s) should:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Be aware of the possible adverse events</td>
</tr>
<tr>
<td>(including delayed and late adverse event)</td>
</tr>
<tr>
<td>- Know what to do in case of adverse event</td>
</tr>
<tr>
<td>- Have a telephone contact to call for advice</td>
</tr>
</tbody>
</table>

Knowledge crucial for home therapy

All patients trained for home therapy should have the following knowledge (9):

- "Know-that" knowledge, which relates to the understanding of the disease, such as diagnosis, prognosis and therapy
- "Know-why" knowledge, which relates to understanding how the patient’s behaviour affects their disease, therapy and daily life
- "Know-how" knowledge, which related to the skills needed to infuse safely

SCIG – self-infusion via pump administration at home for adults

For detailed rationales, please see explanations below the list

Patients should have received immunoglobulin therapy and the dose should be firmly established before starting the training. Patients should fit the inclusion criteria for home therapy.

<table>
<thead>
<tr>
<th>Before the first training session</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Assess the patient's level of understanding of disease, treatment, and technique</td>
</tr>
<tr>
<td>• Describe possible adverse events and assess the patient's knowledge and understanding</td>
</tr>
<tr>
<td>• Complete pre-treatment blood tests (according to local protocol/agreement) (Rationale 1)</td>
</tr>
<tr>
<td>• Immunoglobulin trough levels should be checked regularly, and the patient should know why this is done (Rationale 2)</td>
</tr>
</tbody>
</table>

Pre-infusion assessment

- Teach the patient to assess their well-being, by teaching them not to infuse when they have an infection, flu-like symptoms, or a temperature
- The patient has to assess that the immunoglobulin product ordered is the product prescribed, check the product name, dose, and expiry date
- Show the patient how to inspect the product’s clarity and colour (Rationale 3)
- Remind the patient to verify that the product is at room temperature before the infusion (Rationale 4)
- Teach the patient how to inspect skin and choose infusion site(s) (see Figure)

Figure: SCIG infusion sites
Green areas show preferred infusion sites; other alternatives are shown in blue.

- Advise the patient to have nearby any medication prescribed for use in case of adverse events (NOTE: it is not standard practice in every country to prescribe medication for emergency situations)

**Equipment**
- Immunoglobulin product for subcutaneous use. Please note: doses should be rounded to the nearest whole bottle size, to prevent wastage
- SC infusion pump, able to give adequate infusion rate and pressure
- Needles or mini-spikes and syringes for drawing up the immunoglobulin solution
- Infusion set
- Needle for subcutaneous use, 45° to 90° angle, gauge size 24G to 27G, 6–14 mm length
- Disinfectant
- Gauze
- Adhesive tape
- Sharps container

**Infusion – the patient is educated and trained to (10):**
- Wash hands, prepare a clean area before infusion, and use aseptic technique (Rationale 5)
- Assess their well-being and not to infuse if they have an infection, flu-like symptoms, or a temperature
- When required, complete pre-treatment blood tests and investigations
- Draw the immunoglobulin product into a syringe
- Prime the SC infusion set with immunoglobulin up to 1 cm before the tip of the needle (Rationale 6)
- Clean infusion sites with alcohol wipes and allow to dry (not standard practice in all countries)
- Create a skin fold and insert needle for subcutaneous use into the subcutaneous tissue (at an angle of 45° to 90°, depending on the needle)
- When the needle is placed (and connected to the infusion set), gently pull back the plunger of the syringe to see if any blood flows back into the line. If blood is observed, change infusion set and insert a new needle in another location (Rationale 7)
- Secure the needle with adhesive dressing or use the dressing provided with the needle
- Attach the infusion set to the pump
• At the end of the infusion, remove the needles and dispose of used equipment safely
• Apply post infusion dressing if required
• Assess for adverse events
• Contact emergency services in case of severe adverse events, or the local clinician for milder adverse events
• Complete their infusion log and assess their comfort levels and satisfaction

(Please see troubleshooting in Appendix 6)

**Careful documentation of every SCIG infusion should include:**

• Current health status, medications and any changes in this status in the period between infusions
• The product name, dose and batch numbers of the products used (Rationale 8)
• Any pre-medications taken
• Duration of infusion
• Any problems experienced by the patient during infusion and what was done to address them
• Patient treatment/infusion satisfaction
• The patient should bring their infusion diary to the next appointment with their prescribing clinician

**Rationale 1**
Patients should be tested for exposure to known blood borne pathogens** before** starting SCIG therapy. Once immunoglobulin therapy has been started, serologic tests may become positive because of the passively transferred antibodies and not be informative of the patient's infection status. Normally, health centres test for HIV and hepatitis A, B, and C, and measure complete blood count, hepatic transaminases and renal function before initiating immunoglobulin therapy by any route. In hematologic disease, Coombs' testing should be done prior to SCIG therapy ([www.uptodate.com/contents/general-principles-in-the-use-of-immunoglobulin?source=search_result&search=intravenous+immunoglobulin&slectedTitle](www.uptodate.com/contents/general-principles-in-the-use-of-immunoglobulin?source=search_result&search=intravenous+immunoglobulin&slectedTitle)). In immunodeficient patients, serologic tests are frequently not informative because patients are not able to form antibodies specific for these pathogens. A negative serologic test in a patient with immune deficiency does not mean that the patient has not been exposed to the pathogens. PCR tests are used to detect active infection with Epstein-Barr virus, CMV and Hepatitis B.

**Rationale 2**
To monitor the effectiveness of treatment.

**Rational 3**
The liquid should be clear and transparent; if it is cloudy or has deposits, the product should not be used.

**Rationale 4**
Systemic adverse events are very rare in SC administration, however, they are more likely to occur with cold immunoglobulin solutions (fridge temperature), with the first infusion, a fast infusion, a large infusion, a long interval since the prior infusion, a switch to a new product or batch number, or the presence of a current infection (11). The most common immediate reactions are headache,
cold sweat, light dizziness, chills, fever, and muscular pain. These are usually mild and occur within an hour of starting an infusion and disappear within 6 hours. Both pharmacologic and non-pharmacologic interventions (supplying blankets or pillows, heating pads and encouraging the use of relaxation techniques) may be indicated. Although local reactions are very common with SC administration (local itchiness, swelling and redness) they are deemed normal and are not considered worrisome.

**Rationale 5**
Good hygiene is an important aspect in infection prevention.

**Rationale 6**
When in direct contact with the skin, immunoglobulins can cause local reaction.

**Rationale 7**
Accidental IgG infusion in a blood vessel increases the risk of systemic adverse events.

**Rationale 8**
Although the risk of transmission of blood-borne infections with currently licensed SCIG products is minimal, it is still present. The dose, brand, batch number, expiration date, and manufacturer of any immune globulin product infused into any patient should be carefully recorded in the medical record, as is done for all blood products. In addition, patients should be trained to keep their own logs of this information, as it is often required by law to have donor-to-recipient traceability.

**SCIG – self-infusion via manual push at home for adults**
For detailed rationales, please see explanations below the list

| Patients should have received immunoglobulin therapy and the dose should be firmly established before starting the training. They should fit the inclusion criteria for home therapy. |
|---|---|---|
| **Before the first training session** |
| • Assess patient’s level of understanding of disease, treatment, and technique |
| • Describe possible adverse events and assess the patient’s knowledge and understanding |
| • Complete pre-treatment blood tests (according to local protocol/agreement) (Rationale 1) |
| • Immunoglobulin trough levels should be checked regularly, and the patient should know why this is done (Rationale 2) |
| **Pre-infusion assessment** |
| • Teach the patient to assess their well-being, by teaching them not to infuse when they have an infection, flu-like symptoms, or a temperature |
| • The patient has to assess that the immunoglobulin product ordered is the product prescribed, check the product name, dose, and expiry date |
| • Show the patient how to inspect the product’s clarity and colour (Rationale 3) |
| • Remind the patient to verify that the product is at room temperature before the infusion (Rationale 4) |
| • Teach the patient how to inspect skin and choose infusion site(s) (see Figure) |
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<table>
<thead>
<tr>
<th>Figure: SCIG infusion sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Green areas show preferred infusion sites; other alternatives are shown in blue.</td>
</tr>
</tbody>
</table>

- Advise the patient to have nearby any medication prescribed for use in case of adverse events (NOTE: it is not standard practice in every country to prescribe medication for emergency situations)

<table>
<thead>
<tr>
<th>Equipment</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Immunoglobulin product for subcutaneous use. Please note: doses should be rounded to the nearest whole bottle size, to prevent wastage</td>
</tr>
<tr>
<td>- Needles or mini-spikes and syringes for drawing up the immunoglobulin solution</td>
</tr>
<tr>
<td>- Butterfly needle 23G (blue), approx. 45° insertion angle</td>
</tr>
<tr>
<td>- Disinfectant</td>
</tr>
<tr>
<td>- Gauze</td>
</tr>
<tr>
<td>- Adhesive tape</td>
</tr>
<tr>
<td>- Sharps container</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Infusion – the patient is educated and trained to (10):</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Wash hands, prepare a clean area before infusion, and use aseptic technique (Rationale 5)</td>
</tr>
<tr>
<td>- Assess their well-being and not to infuse if they have an infection, flu-like symptoms, or a temperature</td>
</tr>
<tr>
<td>- When required, complete pre-treatment blood tests and investigations</td>
</tr>
<tr>
<td>- Draw the immunoglobulin into a syringe</td>
</tr>
<tr>
<td>- Not to prime the needle with the immunoglobulin solution (Rationale 6)</td>
</tr>
<tr>
<td>- Clean infusion sites with alcohol wipes and allow to dry (not standard practice in all countries)</td>
</tr>
<tr>
<td>- Create a skin fold and insert needle into the subcutaneous tissue (at an angle of approx. 45°)</td>
</tr>
<tr>
<td>- When the needle is placed, gently pull back the plunger of the syringe to see if any blood flows back. If blood is observed, start over in another location with a new needle (Rationale 7)</td>
</tr>
<tr>
<td>- Inject the immunoglobulin gently, with a rate of 1 mL per minute per site</td>
</tr>
<tr>
<td>- At the end of the infusion, remove the needles and dispose of used equipment safely</td>
</tr>
<tr>
<td>- Apply post infusion dressing if required</td>
</tr>
</tbody>
</table>
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- Assess for adverse events
- Contact emergency services in case of severe adverse events, or the local clinician for milder adverse events
- Complete their infusion log and assess their comfort levels and satisfaction

(Consult troubleshooting in Appendix 6)

**Careful documentation of every SCIG infusion should include:**

- Current health status, medications and any changes in this status in the period between infusions
- The product name, dose and batch numbers of the products used (Rationale 8)
- Any pre-medications taken
- Duration of infusion
- Any problems experienced by the patient during infusion and what was done to address them
- Patient treatment/infusion satisfaction
- The patient should bring their infusion diary to the next appointment with their prescribing clinician

**Rationale 1**
Patients should be tested for exposure to known blood borne pathogens before starting SCIG therapy. Once immunoglobulin therapy has been started, serologic tests may become positive because of the passively transferred antibodies and not be informative of the patient’s infection status. Normally, health centres test for HIV and hepatitis A, B, and C, and measure complete blood count, hepatic transaminases and renal function before initiating immunoglobulin therapy by any route. In hematologic disease, Coombs’ testing should be done prior to SCIG therapy (www.uptodate.com/contents/general-principles-in-the-use-of-immunoglobulin?source=search_result&search=intravenous+immunoglobulin&electedTitle). In immunodeficient patients, serologic tests are frequently not informative because patients are not able to form antibodies specific for these pathogens. A negative serologic test in a patient with immune deficiency does not mean that the patient has not been exposed to the pathogens. PCR tests are used to detect active infection with Epstein-Barr virus, CMV and Hepatitis B.

**Rationale 2**
To monitor the effectiveness of treatment.

**Rationale 3**
The liquid should be clear and transparent; if it is cloudy or has deposits, the product should not be used.

**Rationale 4**
Systemic adverse events are very rare in SC administration, however, they are more likely to occur with cold immunoglobulin solutions (fridge temperature), with the first infusion, a fast infusion, a large infusion, a long interval since the prior infusion, a switch to a new product or batch number, or the presence of a current infection (11). The most common immediate reactions are headache, cold sweat, light dizziness, chills, fever, and muscular pain. These are usually mild and occur within an hour of starting an infusion and disappear within 6 hours. Both pharmacologic and non-pharmacologic interventions (supplying
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blankets or pillows, heating pads and encouraging the use of relaxation techniques) may be indicated. Although local reactions are very common with SC administration (local itchiness, swelling and redness) they are deemed normal and are not considered worrisome.

**Rationale 5**
Good hygiene is an important aspect in infection prevention.

**Rationale 6**
When in direct contact with the skin, immunoglobulins can cause local reaction.

**Rationale 7**
Accidental IgG infusion in a blood vessel increases the risk of systemic adverse events.

**Rationale 8**
Although the risk of transmission of blood-borne infections with currently licensed SCIG products is minimal, it is still present. The dose, brand, batch number, expiration date, and manufacturer of any immune globulin product infused into any patient should be carefully recorded in the medical record, as is done for all blood products. In addition, patients should be trained to keep their own logs of this information, as it is often required by law to have donor-to-recipient traceability.

**fSCIG – self-infusion at home**
Facilitated subcutaneous IgG therapy (fSCIG) is an administration method in which hyaluronidase is injected before subcutaneous IgG (SCIG) to improve the ability of the subcutaneous tissue to accept the immunoglobulin product (12).

Hyaluronidase increases the permeability of the subcutaneous tissue by temporarily depolymerizing hyaluronan. With this method, larger volumes can be dispersed in the subcutaneous space (up to an entire monthly dose at once) than is usually possible with conventional SCIG.

The effect of hyaluronidase is temporary; it remains localized to the treatment area and is fully reversed within 24 to 48 hours.

fSCIG can be given to pregnant women and breast-feeding mothers: clinical experience suggests no harmful effects on the course of pregnancy, on the foetus, or the neonate. Nevertheless, caution should be applied and fSCIG prescribed only if clearly indicated (13).

For detailed rationales, please see explanations below the list
Patients should have received immunoglobulin therapy and the dose should be firmly established before starting the training. Patients should fit the inclusion criteria for home therapy.

### Before the first training session
- Assess patient's level of understanding of disease, treatment, and technique
- Describe possible adverse events and assess the patient's knowledge and understanding
- Complete pre-treatment blood tests (according to local protocol/agreement) (Rationale 1)
- Immunoglobulin trough levels should be checked regularly, and the patient should know why this is done (Rationale 2)

### Pre-infusion assessment
- Teach the patient to assess their well-being, by teaching them not to infuse when they have an infection, flu-like symptoms, or a temperature
- The patient has to assess that the immunoglobulin product ordered is the product prescribed, check the product name, dose, and expiry date
- Show the patient how to inspect the product's clarity and colour (Rationale 3)
- Remind the patient to verify that the product is at room temperature before the infusion (Rationale 4)
- Teach the patient how to inspect skin and choose infusion site(s) (see Figure)

**Figure: fSCIG preferred infusion sites (13)**

- Advise the patient to have nearby any medication prescribed for use in case of adverse events (NOTE: it is not standard practice in every country to prescribe medication for emergency situations)

### Equipment
- Immunoglobulin product for fSCIG (a dual vial unit containing 10% IgG (100 mg/mL) and 160 U/mL human hyaluronidase). Please note: doses should be rounded to the nearest whole bottle size, to prevent wastage
- Infusion pump able to give adequate infusion rate (max. 300 mL per hour) and pressure (≥11.6 psi or 600 mmHg)
- Needles or mini-spikes and syringes for drawing up the hyaluronidase and immunoglobulin solutions
- Infusion set
- Needle for subcutaneous use, gauge size 24G (minimum)
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- Disinfectant
- Gauze
- Adhesive tape
- Sharps container

**Infusion – the patient is educated and trained to:**

- Wash hands, prepare a clean area before infusion, and use aseptic technique (Rationale 5)
- Assess their well-being and not to infuse if they have an infection, flu-like symptoms, or a temperature
- When required, complete pre-treatment blood tests and investigations
- Draw the immunoglobulin into a syringe
- Prime the SC infusion set with immunoglobulin
- Draw the full content of the hyaluronidase vial into a single syringe
- Clean infusion sites with alcohol wipes and allow to dry (not standard practice in all countries)
- Create a skin fold and insert the needle for subcutaneous use into the subcutaneous tissue (at an angle of approx. 45°)
- When the needle is placed and connected to the infusion set, and before the hyaluronidase is injected, gently pull back the plunger of the syringe to see if any blood flows back into the line. If blood is observed, change infusion set and insert a new needle in another location (Rationale 6)
- Secure the needle with adhesive dressing or use the dressing provided with the needle
- Attach the syringe with the hyaluronidase to the subcutaneous needle set
- Administer the hyaluronidase by hand at an initial rate of approx. 1 to 2 mL per minute per infusion site and increase as tolerated
- Within 10 minutes after hyaluronidase administration, attach the infusion set, primed with the immunoglobulin product, to the same needle set used for the hyaluronidase and start the pump according to Table 1 or as discussed with your prescribing clinician

<table>
<thead>
<tr>
<th>Table 1 /SCIG recommended infusion rates (13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunoglobulin 10% for <strong>infusion 3 and subsequent</strong> in patients &gt; 40 kg (&lt; 40 kg)</td>
</tr>
<tr>
<td>Minutes intervals</td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>10 m</td>
</tr>
<tr>
<td>20 m</td>
</tr>
<tr>
<td>30 m</td>
</tr>
<tr>
<td>Remainder of infusion</td>
</tr>
</tbody>
</table>

- At the end of the infusion, remove the needles and dispose of used equipment safely
- Apply post infusion dressing if required
- Assess for adverse events
- Contact emergency services in case of severe adverse events, or the local clinician for milder adverse events
- Complete their infusion log and assess their comfort levels and satisfaction
- Not to do active exercise within 24 hours after infusion
  (Please see troubleshooting in Appendix 6)

**Careful documentation of every /SCIG infusion should include:**

- Current health status, medications and any changes in this status in the period between infusions
- The product name, dose and batch numbers of the products used (Rationale 7)
- Any pre-medications taken
• Duration of infusion
• Any problems experienced by the patient during infusion and what was done to address them
• Patient treatment/infusion satisfaction
• The patient should bring their infusion diary to the next appointment with their prescribing clinician

Rationale 1
Patients should be tested for exposure to known blood borne pathogens before starting SCIG therapy. Once immunoglobulin therapy has been started, serologic tests may become positive because of the passively transferred antibodies and not be informative of the patient’s infection status. Normally, health centres test for HIV and hepatitis A, B, and C, and measure complete blood count, hepatic transaminases and renal function before initiating immunoglobulin therapy by any route. In hematologic disease, Coombs’ testing should be done prior to SCIG therapy (www.uptodate.com/contents/general-principles-in-the-use-of-immunoglobulin?source=search_result&search=intravenous+immunoglobulin&selectedTitle). In immunodeficient patients, serologic tests are frequently not informative because patients are not able to form antibodies specific for these pathogens. A negative serologic test in a patient with immune deficiency does not mean that the patient has not been exposed to the pathogens. PCR tests are used to detect active infection with Epstein-Barr virus, CMV and Hepatitis B.

Rationale 2
To monitor the effectiveness of treatment.

Rationale 3
The liquid should be clear and transparent; if it is cloudy or has deposits, the product should not be used.

Rationale 4
Systemic adverse events are very rare in SC administration, however, they are more likely to occur with cold immunoglobulin solutions (fridge temperature), with the first infusion, a fast infusion, a large infusion, a long interval since the prior infusion, a switch to a new product or batch number, or the presence of a current infection (11). The most common immediate reactions are headache, cold sweat, light dizziness, chills, fever, and muscular pain. These are usually mild and occur within an hour of starting an infusion and disappear within 6 hours. Both pharmacologic and non-pharmacologic interventions (supplying blankets or pillows, heating pads and encouraging the use of relaxation techniques) may be indicated. Although local reactions are very common with SC administration (local itchiness, swelling and redness) they are deemed normal and are not considered worrisome.

Rationale 5
Good hygiene is an important aspect in infection prevention.
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Rationale 6
Accidental IgG infusion in a blood vessel increases the risk of systemic adverse events. Accidental IgG infusion in a blood vessel increases the risk of systemic adverse events, such as thrombolytic events. Accidental hyaluronidase infusion in a blood vessel is not expected to lead to adverse events, as the enzyme is rapidly deactivated in the bloodstream.

Rationale 7
Although the risk of transmission of blood-borne infections with currently licensed immunoglobulin products is minimal, it is still present. The dose, brand, batch number, expiration date, and manufacturer of any immune globulin product infused into any patient should be carefully recorded in the medical record, as is done for all blood products. In addition, patients should be trained to keep their own logs of this information, as it is often required by law to have donor-to-recipient traceability.

References


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13 HyQvia, Summary of Product Characteristics.
7. SCIG self-administration at home – in children

Every country and institution may have different regulations regarding immunoglobulin therapy administration. Some of the steps/measures given below may not be necessary. Please follow your local and national guidelines.

The suitability of each patient for subcutaneous IgG therapy (SCIG) at home needs to be assessed before starting training. The attending doctor, the nurse and the patient, all have to agree to start the training.

Plan the training sessions in a schedule with the patient; advise them that learning the technique might take several sessions.

In children, home-based treatment should always be performed in presence of a parent or legal representative. In the following guideline “the patient” refers to the child and their legal representative.

Criteria for inclusion in a home therapy program
(Please see competency assessment document in Appendix 3 and refer your patients to Appendix 5 for adverse event management at home)

- Patient motivation is important, some patients may never wish to undertake home therapy
- Compliance
- Dexterity, mental capacity and appropriate support should be considered
- A telephone must be available at the place of infusion
- It is advisable that the family doctor is informed of the home therapy
- It is strongly advised that an infusion partner is present at the time of infusion; the infusion partner must also be educated
- The patient and infusion partner should be assessed on a regular basis to verify their knowledge about their condition, their treatment, potential adverse events, and infusion technique. The patient’s compliance with the therapy should also be checked

SCIG is well tolerated by the majority of the patients, but it is important to note that each patient may react differently to different immunoglobulin products. Each patient may also require an individualized infusion regimen in order to minimise adverse events and to achieve the desired therapeutic response (1). SCIG can be given at a frequency varying from daily to every 3–4 weeks (2-4). Once a successful regimen has been established, it should be adhered to at every infusion. Every follow-up visit should include a review of the administration route, premedication and patient treatment satisfaction. A change of route or product may be required; the geographical location of therapy administration may also be changed (hospital or home-therapy).
Local reactions are seen in about 80% of the patients starting with SCIG. The most common are swelling, redness and induration (5). However, these reactions usually subside over time (6). For further information, please refer to the section on adverse event management (Appendix 5).

SCIG can be administered via a pump or manual push (4, 7, 8).

Knowledge crucial for home therapy
All patients trained for home therapy should have the following knowledge (9):

- "Know-that" knowledge, which relates to the understanding of the disease, such as diagnosis, prognosis and therapy
- "Know-why” knowledge, which relates to understanding how the patient’s behaviour affects their disease, therapy and daily life
- “Know-how” knowledge, which related to the skills needed to infuse safely

SCIG – self-infusion via pump administration at home for children
For detailed rationales, please see explanations below the list

<table>
<thead>
<tr>
<th>Patients should have received immunoglobulin and the dose should be firmly established before starting the training. They should fit the inclusion criteria for home therapy.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Before the first training session</strong></td>
</tr>
<tr>
<td>• Assess the level of understanding of disease, treatment, and technique with the child and its legal representative(s)</td>
</tr>
<tr>
<td>• Describe possible adverse events and assess the patient/legal representative’s knowledge and understanding</td>
</tr>
<tr>
<td>• Complete pre-treatment blood tests (according to local protocol/agreement) (Rationale 1)</td>
</tr>
<tr>
<td>• Immunoglobulin trough levels should be checked regularly, and the patient should know why this is done (Rationale 2)</td>
</tr>
<tr>
<td><strong>Pre-infusion assessment</strong></td>
</tr>
<tr>
<td>• Teach the patient/legal representative to assess the patient’s well-being, by teaching them not to infuse when there is an infection, flu-like symptoms, or a temperature</td>
</tr>
<tr>
<td>• The patient/legal representative has to assess that the immunoglobulin product ordered is the product prescribed, check the product name, dose, and expiry date</td>
</tr>
<tr>
<td>• Show the patient/legal representative how to inspect the product’s clarity and colour (Rationale 3)</td>
</tr>
<tr>
<td>• Remind the patient/legal representative to verify that the product is at room temperature before the infusion (Rationale 4)</td>
</tr>
<tr>
<td>• Teach the patient/legal representative how to inspect skin and choose infusion site(s)</td>
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</tbody>
</table>
European Nursing Guidelines for Immunoglobulin Administration

(see Figure)

**Figure: SCIG infusion sites**

Green areas show preferred infusion sites; other alternatives are shown in blue.

- Advise the patient/legal representative to have nearby any medication prescribed for use in case of adverse events (NOTE: it is not standard practice in every country to prescribe medication for emergency situations)

**Equipment**

- Local anaesthetic cream/spray or cryogenic spray may be applied to the SC site (10)
- Immunoglobulin product for subcutaneous use. Please note: doses should be rounded to the nearest whole bottle size, to prevent wastage
- SC infusion pump, able to give adequate infusion rate and pressure
- Needles or mini-spikes and syringes for drawing up the immunoglobulin solution
- Infusion set
- Needle for subcutaneous use, 45° to 90° angle, gauge size 24G to 27G, 6–14 mm length
- Disinfectant
- Gauze
- Adhesive tape
- Sharps container

**Infusion – the patient/legal representative is educated and trained to (11):**

- Wash hands, prepare a clean area before infusion, and use aseptic technique (Rationale 5)
- Assess their well-being and not to infuse if they have an infection, flu-like symptoms, or a temperature
- When required, complete pre-treatment blood tests and investigations
- Draw the immunoglobulin into a syringe
- Prime the SC infusion set with immunoglobulin up to 1 cm before the tip of the needle (Rationale 6)
- Clean infusion sites with alcohol wipes and allow to dry (not standard practice in all countries)
- Create a skin fold and insert needle for subcutaneous use into the subcutaneous tissue (at an angle of 45° to 90°, depending on the needle)
- When the needle is placed (and connected to the infusion set), gently pull back the
plunger of the syringe to see if any blood flows back into the line. If blood is observed, change infusion set and insert a new needle in another location (Rationale 7)

- Secure the needle with adhesive dressing or use the dressing provided with the needle
- Attach the infusion set to the pump
- Do not leave the child unattended during infusion
- At the end of the infusion, remove the needles and dispose of used equipment safely
- Apply post infusion dressing if required
- Assess for adverse events
- Contact emergency services in case of severe adverse events, or the local clinician for milder adverse events
- Complete their infusion log and assess their comfort levels and satisfaction

(Please see troubleshooting in Appendix 6)

**Careful documentation of every SCIG infusion should include**

- Current health status, medications and any changes in this status in the period between infusions
- The product name, dose and batch numbers of the products used (Rationale 8)
- Any pre-medications taken
- Duration of infusion
- Any problems experienced by the patient during infusion and what was done to address them
- Patient treatment/infusion satisfaction
- The patient should bring their infusion diary to the next appointment with their prescribing clinician

**Rationale 1**

Patients should be tested for exposure to known blood borne pathogens before starting SCIG therapy. Once immunoglobulin therapy has been started, serologic tests may become positive because of the passively transferred antibodies and not be informative of the patient's infection status. Normally, health centres test for HIV and hepatitis A, B, and C, and measure complete blood count, hepatic transaminases and renal function before initiating immunoglobulin therapy by any route. In hematologic disease, Coombs' testing should be done prior to SCIG therapy [www.uptodate.com/contents/general-principles-in-the-use-of-immunoglobulin?source=search_result&search=intravenous+immunoglobulin&electedTitle](www.uptodate.com/contents/general-principles-in-the-use-of-immunoglobulin?source=search_result&search=intravenous+immunoglobulin&electedTitle). In immunodeficient patients, serologic tests are frequently not informative because patients are not able to form antibodies specific for these pathogens. A negative serologic test in a patient with immune deficiency does not mean that the patient has not been exposed to the pathogens. PCR tests are used to detect active infection with Epstein-Barr virus, CMV and Hepatitis B.

**Rationale 2**

To monitor the effectiveness of treatment.

**Rational 3**

The liquid should be clear and transparent; if it is cloudy or has deposits, the product should not be used.
Rationale 4
Systemic adverse events are very rare in SC administration, however, they are more likely to occur with cold immunoglobulin solutions (fridge temperature), with the first infusion, a fast infusion, a large infusion, a long interval since the prior infusion, a switch to a new product or batch number, or the presence of a current infection (12). The most common immediate reactions are headache, cold sweat, light dizziness, chills, fever, and muscular pain. These are usually mild and occur within an hour of starting an infusion and disappear within 6 hours. Both pharmacologic and non-pharmacologic interventions (supplying blankets or pillows, heating pads and encouraging the use of relaxation techniques) may be indicated. Although local reactions are very common with SC administration (local itchiness, swelling and redness) they are deemed normal and are not considered worrisome.

Rationale 5
Good hygiene is an important aspect in infection prevention.

Rationale 6
When in direct contact with the skin, immunoglobulins can cause local reaction.

Rationale 7
Accidental IgG infusion in a blood vessel increases the risk of systemic adverse events.

Rationale 8
Although the risk of transmission of blood-borne infections with currently licensed SCIG products is minimal, it is still present. The dose, brand, batch number, expiration date, and manufacturer of any immune globulin product infused into any patient should be carefully recorded in the medical record, as is done for all blood products. In addition, patients should be trained to keep their own logs of this information, as it is often required by law to have donor-to-recipient traceability.

SCIG – self-infusion via manual push at home for children
For detailed rationales, please see explanations below the list

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- Teach the patient/legal representative to assess the patient’s well-being, by teaching them not to infuse when there is an infection, flu-like symptoms, or a temperature
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**Figure: SCIG infusion sites**

![SCIG infusion sites](image)

Green areas show preferred infusion sites; other alternatives are shown in blue.

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- Local anaesthetic cream/spray or cryogenic spray may be applied to the SC site (10)
- Immunoglobulin product for subcutaneous use. Please note: doses should be rounded to the nearest whole bottle size, to prevent wastage
- Needles or mini-spikes and syringes for drawing up the immunoglobulin solution
- Butterfly needle 23G (blue), approx. 45° insertion angle
- Disinfectant
- Gauze
- Adhesive tape
- Sharps container

**Infusion – the patient/legal representative is educated and trained to (11):**

- Wash hands, prepare a clean area before infusion, and use aseptic technique (Rationale 5)
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- When required, complete pre-treatment blood tests and investigations
- Draw the immunoglobulin into a syringe
- Not to prime the needle with the immunoglobulin solution (Rationale 6)
- Clean infusion sites with alcohol wipes and allow to dry (not standard practice in all countries)
- Create a skin fold and insert needle into the subcutaneous tissue in the area that was anesthetized (at an angle of approx. 45°)
- Gently pull back the plunger of the syringe when the infusion needle is placed, to see if any blood flows back. If blood is observed, start over in another location with a new needle (Rationale 7)
- Inject the immunoglobulin gently, with a rate of 1 mL per minute per site
- At the end of the infusion, remove the needles and dispose of used equipment safely
- Apply post infusion dressing if required
- Assess for adverse events
- Contact emergency services in case of severe adverse events, or the local clinician for milder adverse events
- Complete their infusion log and assess their comfort levels and satisfaction
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**Rationale 2**
To monitor the effectiveness of treatment.
European Nursing Guidelines for Immunoglobulin Administration

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Systemic adverse events are very rare in SC administration, however, they are more likely to occur with cold immunoglobulin solutions (fridge temperature), with the first infusion, a fast infusion, a large infusion, a long interval since the prior infusion, a switch to a new product or batch number, or the presence of a current infection (12). The most common immediate reactions are headache, cold sweat, light dizziness, chills, fever, and muscular pain. These are usually mild and occur within an hour of starting an infusion and disappear within 6 hours. Both pharmacologic and non-pharmacologic interventions (supplying blankets or pillows, heating pads and encouraging the use of relaxation techniques) may be indicated. Although local reactions are very common with SC administration (local itchiness, swelling and redness) they are deemed normal and are not considered worrisome.

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Although the risk of transmission of blood-borne infections with currently licensed SCIG products is minimal, it is still present. The dose, brand, batch number, expiration date, and manufacturer of any immune globulin product infused into any patient should be carefully recorded in the medical record, as is done for all blood products. In addition, patients should be trained to keep their own logs of this information, as it is often required by law to have donor-to-recipient traceability.

References


8. IgG therapy during pregnancy

Every country and institution may have different regulations regarding immunoglobulin therapy administration. Please follow your local and national guidelines.

This chapter deals with pregnancy in immunodeficiency rather than in patients receiving immunomodulation therapy.

Immunoglobulin therapy has been safely used in pregnant women with antibody deficiencies. In these cases, the replacement is not only necessary for the mother but also for the foetus. It is imperative for both mother and child that the immunoglobulin treatment is not stopped by anyone other than the initiating clinician (1, 2).

IgG is the only isotype that crosses the placenta during pregnancy, and serum IgG levels in the first few months of life largely represent maternal IgG (3). This is gradually replaced by the infant’s intrinsic IgG and by 6 to 9 months of age the IgG is nearly entirely the infant’s (4).

Patients newly diagnosed with immunodeficiency during pregnancy should be started on immunoglobulin therapy as soon as possible. However, this decision should be made in partnership with the patient.

NOTE: Patients on subcutaneous IgG therapy infusing into their abdomen need to change infusion site as pregnancy progresses (i.e. into the thigh). In fact, the subcutaneous tissue on the abdomen becomes very thigh and “narrow” at end of a pregnancy.

NOTE: fSCIG can be given to pregnant women and breast-feeding mothers: clinical experience suggests no harmful effects on the course of pregnancy, on the foetus, or the neonate. Nevertheless, caution should be applied and fSCIG prescribed only if clearly indicated (5).

The dose during pregnancy should be increased as the mother gains weight. The dose should be kept at ≥100 mg/kg/week (6-9). If there are local or national recommendations regarding the dosing during pregnancy, please follow them.

IgG trough levels should be checked more often during pregnancy and breastfeeding to make sure that they remain adequate, and the patient must be informed about the importance of these measures, because the increase in blood volume can cause inadequate IgG trough levels, which may lead to an increased infection rate (10). The measuring should be done regularly from the second trimester.
If the maternal immunoglobulin therapy is adequate, it has been shown that the new-borns have normal IgG and IgG subclass levels at birth (1).

References


5 HyQvia, Summary of Product Characteristics.


9. Traveling

Every country and institution may have different regulations regarding immunoglobulin therapy administration. Please follow your local and national guidelines.

Short overland travel
Ensure that the patient has been informed to carry an adequate supply of immunoglobulin and equipment with them. Please ensure that they are aware of the temperature restrictions for the storage of the immunoglobulin products.

Travelling abroad
Ensure that the patient has been informed to carry an adequate supply of immunoglobulin and equipment with them. Please ensure that they are aware of the temperature restrictions for the storage of the immunoglobulin products.

Inform the patient that they will require a European Health Insurance Card (EHIC) as well as private travel insurance. The patient will also need a medical certificate stating the necessity of bringing their immunoglobulins and equipment items, and a medical certificate for security and/or customs officials.

It is advisable to provide your patient with an international patient identification card.

Travelling letters or documents are available from different companies and infusion centres.

Travelling by air
The patient must be informed that they should not pack the immunoglobulins in their check-in suitcase, but carry them in their hand luggage; otherwise the immunoglobulins might freeze in the airplane hold and be destroyed. The patient will need a medical certificate stating the necessity of bringing their immunoglobulins and equipment items, and a medical certificate for security and/or customs officials. Please ask patients to contact the airline, and airport security, before the flight to clarify all questions in advance.

Immunoglobulin administration in advance
Immunoglobulin doses can be administered in advance: for example, a patient normally receiving weekly subcutaneous immunoglobulin (SCIG) and not wishing to travel with the equipment, can receive a double immunoglobulin dose before a 2-week trip. Please ask the prescribing clinician for advice on all the possibilities.

An expert on the web!
The patient can find an Expert Immunologist on the website of Jeffrey Model Foundation (JMF) (http://www.info4pi.org/). Some centres supply their patients
with immunoglobulins to be infused locally in the other country. Please refer to your local guideline.
Appendix

1. List of immunoglobulin products

BIVIGAM® (10% solution, Biotest)
Carimune® NF (lyophilised, CSL Behring)
Flebogamma® DIF (5% and 10% solutions, Grifols)
GAMMAGARD® LIQUID (10% solution, Baxalta)
GAMMAGARD® S/D (lyophilised, Baxalta)
GAMMAKED™ (10% solution, Kedrion)
Gammanorm® (16.5% solution, Eurocept)
Gammaplex® (5% solution, BPL)
GammaQuin™ (16% solution, Sanquin)
GAMUNEX®-C (10% solution, Grifols)
Hizentra® (20% solution, CSL Behring)
HyQvia® (recombinant human hyaluronidase with 10% IgG solution, Baxalta)
Kiovig® (10% solution, Baxalta)
Nanogam® (5% solution, Sanquin)
Octagam® (5% and 10% solutions, Octapharma)
Privigen® (10% solution, CSL Behring)
Subcuvia® (16% solution, Baxalta)
European Nursing Guidelines for Immunoglobulin Administration

2. Competency assessment documents for IVIG home therapy

<table>
<thead>
<tr>
<th>Objective</th>
<th>Date Achieved</th>
<th>Assessor</th>
<th>Person Assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STAGE 1</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>1: Rationale for treatment of IVIG</td>
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<td></td>
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<tr>
<td>2: Aseptic technique</td>
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<tr>
<td>3: Identification of equipment</td>
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<td></td>
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</tr>
<tr>
<td>4: Prevention of adverse events</td>
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<tr>
<td><strong>STAGE 2</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1: Record keeping</td>
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<tr>
<td>2: Storage of product</td>
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<tr>
<td>3: Preparation for drug</td>
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<tr>
<td>4: Priming the infusion set</td>
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<tr>
<td>5: Potential problems</td>
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<tr>
<td><strong>STAGE 3</strong></td>
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<td></td>
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</tr>
<tr>
<td>1: Good knowledge of drug administration</td>
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<tr>
<td>2: Calculation of drip rate</td>
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<tr>
<td><strong>STAGE 4</strong></td>
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<tr>
<td>1: Flushing of peripheral line</td>
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<td>2: Safe removal of butterfly needle</td>
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<tr>
<td>3: Safe disposal of equipment</td>
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<tr>
<td><strong>STAGE 5</strong></td>
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<tr>
<td>1: Difference between veins and arteries</td>
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<tr>
<td>2: Selection of veins for IVIG</td>
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<tr>
<td>3: Venepuncture</td>
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<tr>
<td>4: Dealing with potential problems</td>
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<tr>
<td><strong>STAGE 6</strong></td>
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<tr>
<td>1: Reason for blood sampling</td>
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<td>2: Blood sampling</td>
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<td>3: Completing request forms, labelling sampling and posting samples</td>
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<tr>
<td><strong>STAGE 7</strong></td>
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<tr>
<td>1: Possible reactions to IVIG</td>
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<td><strong>STAGE 8</strong></td>
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<tr>
<td>1: Obtaining supply and prescriptions</td>
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3: Contract / Consent

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<tr>
<th>STAGE 9</th>
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<tbody>
<tr>
<td>1: Monitor learning</td>
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<tr>
<td>2: Motivate the patient and carer</td>
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<td>3: Judge the level of patient and carer achievement</td>
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<td>5: Measure the effectiveness of teaching</td>
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<td></td>
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</tr>
<tr>
<td>1: Selection of area for SCIG</td>
<td></td>
<td></td>
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<tr>
<td>2: Dealing with potential problems</td>
<td></td>
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</tr>
<tr>
<td><strong>STAGE 5</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1: Safe removal of butterfly needle</td>
<td></td>
<td></td>
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<tr>
<td>2: Safe disposal of equipment</td>
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<tr>
<td><strong>STAGE 6</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>1: Safe use of the syringe driver</td>
<td></td>
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<tr>
<td>2: Maintenance of the syringe driver</td>
<td></td>
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<tr>
<td><strong>STAGE 7</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1: The reason for blood sampling</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>2: Blood sampling</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>3: Completing request forms</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>labelling and posting the sample</th>
</tr>
</thead>
</table>

**STAGE 8**

1: Possible reactions to SCIG
2: Knowledge of how to reduce the risks of adverse events
3: How to manage adverse events

**STAGE 9**

1: Possible GP involvement
2. Emergency care
3: Contract/consent

**STAGE 10**

1: Monitor learning
2: Motivate the patient and carer
3: Judge the level of patient and carer achievement
4: Enable the patient and carer to participate in home therapy
5: Measure the effectiveness of teaching
### 4. Systemic adverse event management for hospital-based treatment

The recommendations provided in the table below are valid for IVIG and SCIG therapies.

<table>
<thead>
<tr>
<th>Event</th>
<th>Severity</th>
<th>Nursing Interventions</th>
</tr>
</thead>
</table>
| Non IgE mediated anaphylaxis or anaphylaxis | Non IgE mediated anaphylaxis or anaphylaxis (very rare) | • Follow your local guidelines  
• Can be prevented by waiting a couple of days before infusion if your patient has fever and/or an acute infection  
• You must ensure patients know the signs of anaphylaxis onset |
| Chills/rigors                               | Mild     | • Slow down the infusion  
• Take temperature (chills) or blood pressure and temperature (rigors)  
• Administer prescribed medications  
• When symptoms resolve, restart the infusion at the slowest rate |
|                                            | Moderate | • Stop the infusion  
• Take temperature (chills) or blood pressure and temperature (rigors)  
• Administer prescribed medications  
• When symptoms resolve, restart the infusion at the slowest rate  
• Inform the doctor |
|                                            | Severe   | • Stop the infusion  
• Follow local guidelines for severe adverse events and follow steps recommended for moderate chills/rigors |
| Headache                                   | Mild     | • Inform the patient this can happen  
• Make sure the patient is adequately hydrated  
• Administer painkiller if required  
• Reduce rate  
• Observe  
NOTE: advise patients on IVIG therapy to drink more water than usual in the 24 hours before the next infusion |
## European Nursing Guidelines for Immunoglobulin Administration

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
</table>
|                         | Moderate| Make sure patients on IVIG therapy are adequately hydrated on the day of the infusion.  
|                          |        | • Administer painkiller if required  
|                          |        | • Reduce rate  
|                          |        | • Call the doctor                                                        |
|                         | Severe | Stop the infusion  
|                          |        | • Administer painkiller  
|                          |        | • Call the doctor                                                        |
|                         |        | • If the patient calls 24 to 72 hours later with photosensitivity/photophobia and neck stiffness, meningitis needs to be excluded |
| Urticaria/Hives         | Moderate| Inform the patient this can happen  
|                          |        | • Stop the infusion  
|                          |        | • Administer anti-histamines  
|                          |        | • Take temperature and blood pressure to make sure this event is not the onset of anaphylaxis  
|                          |        | • Observe the rash  
|                          |        | • Call the prescriber  
|                          |        | • Restart the infusion at slower rates                                      |
|                         | Severe | Stop the infusion  
|                          |        | • Administer anti-histamines  
|                          |        | • Call the doctor                                                        |
|                          |        | • Take temperature and blood pressure to make sure this event is not the onset of anaphylaxis |
| Nausea/Vomiting         | Mild   | Inform the patient this can happen  
|                          |        | • Observe  
|                          |        | • Be aware that this could be the onset of anaphylaxis                      |
|                         | Moderate| Stop the infusion  
|                          |        | • Observe  

### Back pain

<table>
<thead>
<tr>
<th>Severity</th>
<th>Actions</th>
</tr>
</thead>
</table>
| **Mild** | • Inform the patient this can happen  
• Observe  
• Be aware that this could be the onset of anaphylaxis |
| **Moderate** | • Slow down or stop the infusion  
• Observe  
• Give the patient painkillers  
• Be aware that this could be the onset of anaphylaxis |
| **Severe** | • Stop the infusion  
• Give the patient anti-sickness medication  
• Call the doctor  
• Take temperature and blood pressure to make sure this event is not the onset of anaphylaxis |

### Local reactions in SCIG (swelling, redness, induration, itching, burning)

<table>
<thead>
<tr>
<th>Severity</th>
<th>Actions</th>
</tr>
</thead>
</table>
| **Mild** | • Inform the patient that this is expected during the first 8–10 infusions but that the local reactions will decline  
• Observe and document |
| **Moderate** | • Observe and document  
• Maybe administer anti-histamines |
| **Severe** | • Stop the infusion  
• Administer anti-histamines  
• Call the doctor |
European Nursing Guidelines for Immunoglobulin Administration

- Check for allergies to dressings, cleaning solutions, tape, latex
- Record batch number

Please note that thrombolytic events and neutropenia can occur when IVIG therapy is used at large doses or in immobile patients. Manage them according to your local guidelines.
5. **Adverse event management for home-based treatment**

The recommendations provided in the table below are valid for IVIG and SCIG therapies.

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Severity</th>
<th>Home Interventions</th>
</tr>
</thead>
</table>
| **Non IgE mediated anaphylaxis or anaphylaxis (very rare)** | Mild | • Call emergency services immediately  
• Record batch number and inform your infusion centre |
| | Moderate | • Stop infusion  
• Take painkiller  
• Record batch number and inform your infusion centre  
• See your doctor immediately or call an ambulance  
• The next infusion must take place in your infusion centre |
| | Severe | • Stop infusion  
• Call emergency services immediately  
• Record batch number and inform your infusion centre  
• The next infusion must take place in your infusion centre |
| **Chills/rigors** | Mild | • Stop infusion  
• Take painkiller  
• Record batch number and inform your infusion centre |
| | Moderate | • Stop infusion  
• Take painkiller  
• See your doctor immediately or call an ambulance  
• Record batch number and inform your infusion centre  
• The next infusion must take place in your infusion centre |
| | Severe | • Stop infusion  
• Call emergency services immediately  
• Record batch number and inform your infusion centre  
• The next infusion must take place in your infusion centre |
| **Headache** | Mild | • Make sure you are adequately hydrated  
• Administer painkiller if required  
• Reduce the rate and use a slower rate during next infusion  
**NOTE:** drink more water than usual in the 24 hours before the next infusion |
<table>
<thead>
<tr>
<th>Condition</th>
<th>Level</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>European Nursing Guidelines for Immunoglobulin Administration</td>
<td></td>
<td><strong>Moderate</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Make sure you are adequately hydrated on the day of the infusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Administer painkiller if required</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Stop the infusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Inform your infusion centre</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• See your doctor immediately</td>
</tr>
<tr>
<td></td>
<td><strong>Severe</strong></td>
<td>• Stop the infusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Call emergency services immediately</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Record batch number and inform your infusion centre</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• The next infusion must take place in your infusion centre</td>
</tr>
<tr>
<td>Urticaria/Hives</td>
<td><strong>Moderate</strong></td>
<td>• Stop the infusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Take anti-histamines</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Observe the rash, take photos</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• See your family doctor immediately or seek emergency services</td>
</tr>
<tr>
<td></td>
<td><strong>Severe</strong></td>
<td>• Stop the infusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Call emergency services immediately</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Record batch number and inform your infusion centre</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• The next infusion must take place in your infusion centre</td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td><strong>Mild</strong></td>
<td>• Observe</td>
</tr>
<tr>
<td></td>
<td><strong>Moderate</strong></td>
<td>• Stop the infusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Observe</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Call your infusion centre</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Take anti-sickness medication</td>
</tr>
<tr>
<td></td>
<td><strong>Severe</strong></td>
<td>• Stop the infusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Call emergency services immediately</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Record batch number and inform your infusion centre</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• The next infusion must take place in your infusion centre</td>
</tr>
<tr>
<td>Back pain</td>
<td><strong>Mild</strong></td>
<td>• Slow down the infusion</td>
</tr>
</tbody>
</table>
### European Nursing Guidelines for Immunoglobulin Administration

<table>
<thead>
<tr>
<th>Infusion Reaction</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infusion Reaction</td>
<td>Observe</td>
<td>Take a photo of the reaction</td>
<td>Stop the infusion</td>
</tr>
<tr>
<td></td>
<td>Take a photo of the reaction</td>
<td>Administer anti-histamines</td>
<td>Take anti-histamines</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Call emergency services immediately</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Record batch number and inform your infusion centre</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Your next infusion will need to take place at your infusion centre</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Local reactions in SCIG (swelling, redness, induration, itching, burning)</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infusion Reaction</td>
<td>Observe</td>
<td>Take a photo of the reaction</td>
<td>Stop the infusion</td>
</tr>
<tr>
<td></td>
<td>Take a photo of the reaction</td>
<td>Administer anti-histamines</td>
<td>Take anti-histamines</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Call emergency services immediately</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Record batch number and inform your infusion centre</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Your next infusion will need to take place at your infusion centre</td>
</tr>
</tbody>
</table>
6. Troubleshooting

To avoid problems during infusion it is very important to inspect carefully the area before needle insertion. Look for nodules in subcutaneous tissue, oedema (SCIG), haematoma, fibrosed veins (IVIG) or irritated skin/rash. Please also check the tables on adverse event management (Appendix 4 and 5). The in the following table the following format is used: “what to check: how to act”.

In SCIG therapy most local problems after the first 8–10 infusions are caused by the use of too short needles.

<table>
<thead>
<tr>
<th>Problem</th>
<th>IVIG</th>
<th>SCIG</th>
<th>/SCIG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leaky site</td>
<td>• Needle: correct position</td>
<td>• Needle: correct position, length, diameter</td>
<td>• Needle: correct position, length, diameter</td>
</tr>
<tr>
<td></td>
<td>• Connections: tighten</td>
<td>• Connections: tighten</td>
<td>• Connections: tighten</td>
</tr>
<tr>
<td></td>
<td>• Fixation: secure dressing/ tape/bandage</td>
<td>• Fixation: secure dressing/ tape/bandage</td>
<td>• Fixation: secure dressing/ tape/bandage</td>
</tr>
<tr>
<td></td>
<td>• Integrity of equipment</td>
<td>• Volume: decrease per site</td>
<td>• Volume: decrease per site</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Infusion rate: slow down</td>
<td>• Infusion rate: slow down</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Integrity of equipment</td>
<td>• Integrity of equipment</td>
</tr>
<tr>
<td>Discomfort/pain at infusion site</td>
<td>• Needle: correct position</td>
<td>• Needle: dry needle insertion. Needle too short or too long? Movement of needle? Change type, brand and/or length of needle</td>
<td>• Needle: dry needle insertion. Needle too short or too long? Movement of needle? Change type, brand and/or length of needle</td>
</tr>
<tr>
<td></td>
<td>• Fixation: secure dressing/ tape/bandage</td>
<td>• Fixation: secure dressing/ tape/bandage</td>
<td>• Fixation: secure dressing/ tape/bandage</td>
</tr>
<tr>
<td></td>
<td>• Extravasation: start over</td>
<td>If you can’t resolve the problem, remove needle and start again with a new needle/location</td>
<td>If you can’t resolve the problem, remove needle and start again with a new needle/location</td>
</tr>
<tr>
<td>Blood at the infusion site or in the line, before starting the infusion</td>
<td>• This is normal, you are in the correct position</td>
<td>• Blood at the site only (none in the line): proceed to infusion</td>
<td>• Blood (even small amounts) at puncture site or in the line: remove the needle and start again with a new needle in a new location (there might be a risk of severe haematoma due to the</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Blood in the line: remove the needle and start again with a new needle in a new location. In case of multi-site lines, you may clamp the site, which has blood in the line,</td>
<td></td>
</tr>
<tr>
<td><strong>Local reactions</strong> (swelling, redness, induration, itching, burning)</td>
<td><strong>and infuse through the remaining ports if you consider the change of volume per site will not be a problem</strong></td>
<td><strong>hyaluronidase)</strong></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>• Needle: correct position</td>
<td>• Infusion site: inform the patient that local reactions are expected after the first 8–10 infusions and usually resolve between 12 and 72 hours</td>
<td>• Infusion site: inform the patient that local reactions are expected and usually resolve between 12 and 72 hours</td>
<td></td>
</tr>
<tr>
<td>• Connections: tighten</td>
<td>• Volume: decrease per site</td>
<td>• Volume: decrease per site</td>
<td></td>
</tr>
<tr>
<td>• Fixation: secure dressing/ tape/bandage</td>
<td>• Infusion rate: slow down</td>
<td>• Infusion rate: slow down</td>
<td></td>
</tr>
<tr>
<td>• Integrity of equipment: replace if necessary</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Allergies to any used products: change equipment, anti-histamine can be given, inform a doctor</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
7. Levels of evidence in clinical and medical literature

<table>
<thead>
<tr>
<th>LEVELS OF EVIDENCE (1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy/Prevention/Aetiology/Harm</td>
</tr>
<tr>
<td>1a Systematic reviews (with homogeneity) of randomized controlled trials</td>
</tr>
<tr>
<td>1b Individual randomized controlled trials (with narrow confidence interval)</td>
</tr>
<tr>
<td>1c All or none randomized controlled trials</td>
</tr>
<tr>
<td>2a Systematic reviews (with homogeneity) of cohort studies</td>
</tr>
<tr>
<td>2b Individual cohort study (including low-quality randomized controlled trials; e.g., &lt; 80% follow-up)</td>
</tr>
<tr>
<td>2c &quot;Outcomes&quot; research; ecological studies</td>
</tr>
<tr>
<td>3a Systematic reviews (with homogeneity) of case-control studies</td>
</tr>
<tr>
<td>3b Individual case-control study</td>
</tr>
<tr>
<td>4 Case-series (and poor quality cohort and case control studies)</td>
</tr>
<tr>
<td>5 Expert opinion without explicit critical appraisal, or based on physiology, bench research or &quot;first principles&quot;</td>
</tr>
</tbody>
</table>