Primary immunodeficiencies

Plasma-derived therapies

IPOPI
INTERNATIONAL
PATIENT ORGANISATION
FOR PRIMARY IMMUNODEFICIENCIES

List of some common abbreviations	
C1-INH	C1 esterase inhibitor
CVID	Common variable immunodeficiency
HAE	Hereditary angioedema
Hyper IgM	X-linked hyperimmunoglobulin M syndrome
IG	Immunoglobulin (antibody)
IV	Intravenous
PID	Primary immunodeficiencies
SC	Subcutaneous
SCID	Severe combined immunodeficiency
WAS	Wiskott-Aldrich syndrome
XLA	X-linked (or Bruton's) agammaglobulinaemia

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Introduction

This booklet describes the plasma-derived therapies used to treat primary immunodeficiencies.

Primary immunodeficiencies (PIDs) are a group of rare diseases caused by some components (mainly cells and/or proteins) of the immune system not working properly. The immune system normally helps protect the body from infections caused by micro-organisms, such as bacteria, viruses or fungi. People with PIDs are therefore more likely than other people to catch infections.

Most PIDs cause the body to produce too few or no functioning immunoglobulins (IGs), also known as antibodies. IGs are an important part of the immune system as they recognise and attack the micro-organisms that can cause infections.

Plasma-derived therapies are life-saving treatments used to treat various rare conditions, including PIDs. They are developed from donated human plasma. Immunoglobulin replacement therapy (IG Therapy) is the main plasma-derived therapy used to treat PIDs. It contains IGs from the healthy donors, which help to protect against a range of infections and reduce autoimmune symptoms. It is used to treat various PIDs, including:

- common variable immunodeficiency (CVID)
- X-linked agammaglobulinaemia (XLA)
- X-linked hyperimmunoglobulin M syndrome (hyper IgM)
- Wiskott-Aldrich syndrome (WAS)
- severe combined immunodeficiency (SCID) and other combined immunodeficiencies.

IG replacement therapy is a life-long, life-saving treatment and, as PIDs are chronic conditions, it needs to be administered regularly. It is important that you do not miss or forget to receive your treatment as each treatment only provides temporary protection against infections.

Another type of plasma-derived therapy is used specifically to treat patients with hereditary angioedema (HAE). In people living with this condition, a component of the immune system called C1 esterase inhibitor (C1-INH) is missing or malfunctioning and plasma-derived C1-INH concentrate may be prescribed to prevent and treat the symptoms of inflammation associated with HAE.

Early diagnosis and access to appropriate treatments enables many patients with PIDs to lead full and active lives.

Importance of physician choice and patient preferences

Treatments for PIDs are generally available from centres with specialist knowledge of diagnosing and treating people with PIDs. The type of treatment you receive will depend on a number of factors, including your PID type and whether you have any other medical conditions.

A number of plasma-derived therapies are available and, as they are biological products, they all have unique qualities. While they are all effective therapies, differences in the way they are developed affect, for example, their suitability for individual patients, the time it takes to administer them and potential side-effects. Plasma-derived therapies are not generic medicines.

It is important that you are aware of all the treatments options and discuss the most appropriate therapy for your condition with your doctor. Families and carers should also be involved in supporting these decisions.

You may consider the following aspects to be important for your PID treatment:

- effectiveness
- length of time between treatments
- side-effects
- administration time
- home or hospital/clinic delivery
- ability to self-administer with training
- ease of use
- safety
- painless.

Receiving IG replacement therapy

IG replacement therapy is given as an infusion (or 'drip') either intravenously (IV) or subcutaneously (SC).

IV route: This involves infusing IG straight into your blood stream through a vein. The main advantage of this route is that a higher dose of IG can be given compared with the SC route and therefore treatment only needs to be given every 3 or 4 weeks. However, each infusion can take 2–4 hours to administer and is usually given by a doctor or nurse in a hospital or clinic. A nurse or trained carer can also give it at home. Mild side-effects may occur during or after IV infusions (for more details see side effects section)

SC route: With the SC route, IG is infused just under the skin of your upper arm, abdomen, thighs or buttocks using either a portable infusion pump ('syringe driver') or a rapid push technique. The rapid push technique is a simple method that uses a syringe to push the IG under the skin at a rate that is comfortable for you.

Each SC infusion takes less time (1–2 hours) than an IV infusion so is more likely to fit into your normal daily schedule, which may be more convenient. However, as this route can administer only small doses of IG, it is usually given at least once a week. Larger doses can be given using more than one injection site. You or your carer can carry out SC infusions at home after training by your medical team. If you or your carer do wish to administer IG, you must be willing and able to keep to the dosing schedule and keep a treatment diary. Compliance and the ability to self administer are important in deciding whether this is the best route.

	IV route	SC route
How long	2–4 hours	Infusion pump: 1–2 hours Rapid push: 5–20 minutes
How often	Every 3–4 weeks	Infusion pump: At least once a week (every 2–3 weeks for small children/infants) Rapid push: More often
Where	Usually clinic	At home
Side-effects	Some patients may feel unwell during or right after treatment	Occasional pain and swelling at injection site

What are the possible side-effects?

Most patients do not experience serious side-effects from IG replacement therapy, however, some patients may experience the following:

- headache
- lightheaded, fainting or feeling faint
- chills, fever
- feeling or being sick
- itching, redness of skin
- joint pains
- rapid heart beat.

These side-effects are less common with the SC route of administration than the IV route. However, SC infusions can cause some swelling and pain at the injection sites.

Most side-effects respond to slowing the infusion rate and ensuring good hydration before and during treatment (alcohol intake should be limited to avoid dehydration).

Side-effects are more common when there is an underlying infection requiring treatment. It is, therefore, very important to tell your doctor if you are feeling unwell.

More severe side-effects, such as aseptic meningitis, loss of red blood cells (haemolytic anaemia), thromboembolic events (blood clots) and serious allergic reactions, are extremely rare.

You should watch out for signs of infection and report them quickly to your doctor.

Travelling

You should also make sure that you are well prepared if you intend to travel internationally and discuss any travel plans with your doctor in good time.

Hereditary angioedema

Hereditary angioedema is an inherited disorder caused by levels of the protein C1-INH being either too low or not working properly. C1-INH helps manage inflammation in the body by controlling C1, which is the first component of the complement system (part of the immune system). The disease causes acute attacks of swelling that may affect various parts of the body such as the hands, feet, face, airways and intestines. These attacks can last for several days. Swelling of the airways is particularly dangerous and requires immediate treatment. Some people suffer attacks once or twice a year; others experience them every few days. While the triggers for HAE attacks are not completely understood, it is known that minor trauma, infections and stress can lead to attacks.

Plasma-derived C1-INH products can be used to prevent and treat HAE attacks. They need to be injected or infused by the IV route either in a hospital/clinic or at home. You or your carer can perform this once you have received the required medical training. An alternative genetically engineered (recombinant) C1-INH product is also available.

Swelling of the airways can be potentially fatal so it is important that you receive treatment as soon as you experience the early symptoms of an attack.

Therapeutic options

IGs are available in most countries and the International Patient Organisation for Primary Immunodeficiencies (IPOPI) has compiled a comprehensive country-by-country list of IG products, which can be found on its website at www.ipopi.org.

Each product has slightly different characteristics so some products may be more appropriate for you than others. Your doctor will be able to discuss this with you before deciding on your treatment.

The characteristics of an IG product that need to be considered are as follows:

IgA levels	The level should be as low as possible for patients with a history of severe allergic reactions
Infusion route	The SC route may be more appropriate for patients who prefer treatment that can be administered at home, or for patients with poor venous access The IV route may be more appropriate for some adults due to the longer time between treatments, or for patients who may not want to self-administer. Patients with other health issues or who find it difficult to keep to a dosing schedule may benefit from receiving their treatment in a clinical setting.
Fluid load	Avoid in patients with fluid restrictions and in infants
Stabilisers	Sugars and amino acids are added to IGs to stabilise them
Sucrose	Avoid in patients at risk of kidney complications
Glucose	Avoid in patients with diabetes
Amino acids	Avoid in patients with history of severe allergic reactions and certain metabolic disorders
Sodium	Avoid in patients at cardiovascular risk
High concentration	Avoid in patients at cardiovascular risk and in infants

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How are IG therapies produced?

IG therapies are made from human plasma donated by healthy individuals. IG levels normally vary in healthy people so plasma is obtained from a large number of donors to ensure that it contains the highest concentration of antibodies.

As IG therapies are sourced from either blood (recovered plasma) or plasma (source plasma) donations, it is very important that they are safe to use and free from micro-organisms that may cause infections. IG therapies have an excellent safety record. While all biological products carry a very small risk of infection, the risk with immunoglobulins is minimised by the following steps:

Donor selection: Selection procedures ensure that donors are healthy

Testing: Donations are tested and contaminated donations rejected

Virus elimination: Additional steps during the production process ensure viruses are inactivated and/or removed.

Further information and support

This booklet has been produced by IPOPI. Other booklets are available in this series. For further information and details of PID patient organisations in 47 countries worldwide, please visit **www.ipopi.org**.

Provided by IMMUNO DEFICIENCY UK

Supporting families affected by primary and secondary immunodeficiency

Immunodeficiency UK is a national organisation supporting individuals and families affected by primary and secondary immunodeficiency.

We are the UK national member of IPOPI, an association of national patient organisations dedicated to improving awareness, access to early diagnosis and optimal treatments for PID patients worldwide.

Our website has useful information on a range of conditions and topics, and explains the work we do to ensure the voice of patients with primary and secondary immunodeficiency is heard. If we can be of any help, please email us or call on the number above, where you can leave a message.

Support us by becoming a member of Immunodeficiency UK. It's free and easy to do via our website. Members get monthly bulletins.

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www.immunodeficiencyuk.org
hello@immunodeficiencyuk.org
0800 987 8986