

Immunoglobulin therapy

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



PID UK

Supporting families affected
by primary immunodeficiencies

About this booklet

This booklet provides information on immunoglobulin therapy (Ig therapy). It has been produced by the PID UK Medical Advisory Panel and Patient Representative Panel to help answer the questions patients and their families may have about this treatment for people affected by primary immunodeficiency but should not replace advice from a clinical immunologist.

Contents

What is immunoglobulin replacement therapy?	3
What is the difference between intravenous and subcutaneous immunoglobulin?	3
Will I be given the choice between intravenous and subcutaneous immunoglobulin?	3
What is in the immunoglobulin?	4
Why do I need immunoglobulin?	4
What tests do I need to have before starting immunoglobulin?	4
I heard that some people have reactions to immunoglobulins	5
Are there any other safety problems with immunoglobulin?	5
What do the manufacturers do to make sure there are no infections in the immunoglobulin?	6
What kind of follow-up should I expect if I start immunoglobulin?	7
Why is it important to record the batches of immunoglobulin?	8
Is it possible I don't need immunoglobulin anymore?	8
What products are available?	8
How do hospitals ensure they don't run out of immunoglobulin?	8
What if I want to go on holiday?	9
How do I ensure I'm doing home therapy safely?	9
Who can I contact if I want to discuss my treatment?	9
Provision of immunoglobulin within the NHS	10
Clinical guidelines for immunoglobulin use	11
More questions about immunoglobulin therapy?	11
Glossary of terms	12

Immunoglobulin therapy. First edition April 2015.

© Primary Immunodeficiency UK (PID UK), April 2015. Published by PID UK (www.piduk.org)

What is immunoglobulin replacement therapy?

Immunoglobulin replacement therapy is a blood-based treatment. The immunoglobulin contains antibodies that help to fight infection. You have been recommended this treatment because your doctors have found that your immune system (or your child's immune system) is not making antibodies. Immunoglobulin can be given intravenously or subcutaneously.

What is the difference between intravenous and subcutaneous immunoglobulin?

Intravenous immunoglobulin (IVIG) has been in use since the 1970s and involves giving immunoglobulin straight into the circulation system by a needle in a vein. Quite large amounts of immunoglobulin can be given this way and for this reason treatment is only needed every three weeks or so, with each treatment lasting between two and four hours. If you have side effects with IVIG it is usually because it is being given too quickly. Initially you would have treatment in hospital, but most people can be trained to have it at home.

Subcutaneous immunoglobulin (SCIG) has been developed more recently than IVIG, with new immunoglobulin preparations being produced exclusively for subcutaneous use by 2005. In SCIG, immunoglobulin is delivered by a needle into the fatty tissues under the skin, where it enters the circulation slowly over a few days. There isn't much room under the skin, so the dose of immunoglobulin given is smaller than with IVIG. For this reason, SCIG is usually given every week. Nearly everybody on SCIG learns how to have treatment at home, with each session lasting up to about two hours.

Will I be given the choice between intravenous and subcutaneous immunoglobulin?

Your immunology team will give you the information to help you decide which treatment you will have. You might want to consider the following factors:

- If you have really 'bad' veins, then IVIG may not be your best option.
- If you want to take ownership of your illness, then SCIG may be the best choice because you will probably learn how to have home therapy faster.
- Infusion-related side effects are more common with IVIG than SCIG and can be related to the volume and rate of infusion.

Your immunology centre will be able to offer you either treatment depending on these factors and your personal choice. Across the UK about 60 per cent of people with immune deficiency are on IVIG.

What is in the immunoglobulin?

Immunoglobulin is made from donated blood-derived plasma. During manufacture everything except a type of immunoglobulin called immunoglobulin G (IgG) is removed from the plasma. IgG is very good at fighting bacteria and viruses. IgG has other effects too, so it isn't just used for people with immune deficiency. You might hear about immunoglobulin being used in some people with other immune (autoimmune) problems.

Why do I need immunoglobulin?

Immune-deficient patients are at a greater risk of infection than others. Clinical trials have shown that for people with immune deficiency, immunoglobulin treatments result in fewer infections, and the infections that do occur tend to be less serious. There is also evidence that people with immune deficiency are more likely to enjoy good health over many years if they receive immunoglobulin correctly. Finally, your wellbeing and energy levels are likely to be better if you are on immunoglobulin. Please note that it may take several months before you feel these benefits.

What tests do I need to have before starting immunoglobulin?

Your immunologist will only recommend starting immunoglobulin if you have had tests which confirm it is the right treatment for you. In cases of severe immune deficiency, only a couple of blood tests are required before the doctor will recommend immunoglobulin.

Fortunately, most people have mild immune deficiency and in this situation the doctor might try other treatments before immunoglobulin. For example, the immunologist might try giving you vaccines and checking how well you respond. This 'vaccine challenge' can take several weeks as you have to have the vaccine, wait a few weeks before the blood tests and then get the results.

Your immunologist might suggest taking regular antibiotics for a few months and seeing how well these protect you from infection. This can be done while you wait for the results of a vaccine challenge.

Finally, your immunologist might suggest trying immunoglobulin for a period of time, for example, a year. If it is clear that you have benefitted, then your immunologist will recommend you continue it, but if you do not benefit he or she will suggest stopping.

I heard that some people have reactions to immunoglobulins

Most people do not have reactions to immunoglobulins. This is why it is safe to go on to home therapy.

The reactions that do sometimes happen include rashes, a high temperature, shivering or itching. You can also get a headache with immunoglobulin, although this tends to happen the day after it is given.

When reactions do happen, there is usually one of two factors responsible:

- Immunoglobulin is given too fast for the individual concerned. This is most likely to happen with IVIG because a larger dose is being given. If you have a reaction during an infusion, the first thing to do is to slow the infusion right down and consider stopping it if the symptoms do not improve rapidly. Once recovered, you should record the details of the reaction in order to inform your clinical immunology team.
- Immunoglobulin is given at a time when there is an infection. If you have a cold or a chest infection on the day of your infusion, you are more likely to have a reaction. Immunology teams will help you recognise the symptoms of infection, so that you can delay your infusion by a couple of days if necessary. Because immunoglobulin treatment takes a few months to reduce the risk of infections, this is most likely to happen when you have just started immunoglobulin.

If you continue to have reactions with immunoglobulin, your immunologist may recommend taking paracetamol or antihistamines first. Sometimes reactions occur with one batch of immunoglobulin but these may go away once the batch is changed. Very occasionally your immunologist will recommend you change your immunoglobulin product because reactions cannot be brought under control.

If you have reactions when you start immunoglobulin treatment, the chances are that they will be brought under control.

Are there any other safety problems with immunoglobulin?

Immunoglobulin is made from blood donations. Several thousand blood donations are pooled in the process. For these reasons there is always a possibility of catching an infection from one of the blood donors.

No one has ever caught HIV or hepatitis B from immunoglobulin therapy. In the 1990s, a small number of people caught hepatitis C from immunoglobulin. These days, blood donors are selected very carefully and the manufacturing process contains steps to remove viruses and bacteria.

There have been no cases of infection being spread from person to person by immunoglobulin since the 1990s.

There are two theoretical risks from immunoglobulin. The first is from prion infection. Prions cause BSE (mad cow disease) and variant CJD, mainly in the UK. Prions have been spread from person to person by blood transfusions but never by immunoglobulin. But because of this theoretical risk, British plasma is not used for making immunoglobulin.

The other risk is of new infections that start to affect humans, either because of global climate change or change in behaviour (e.g. feeding sheep to cows, in the case of BSE). One example of this is a virus that affected people in New York and entered the blood supply there.

It is very difficult to predict whether new infections, which could be spread by immunoglobulin, will appear in the future. However, the immunoglobulin manufacturers and immunologists around the world are constantly on the lookout for any problems such as this.

What do the manufacturers do to make sure there are no infections in the immunoglobulin?

The first step the manufacturers take is to get to know the blood donors really well. Manufacturers insist that their donors donate regularly. Each time a donor attends the blood centre they are asked a lot of questions, ranging from their sex lives to any recent travel. They then donate the blood as well as having a series of blood tests to make sure they don't have an infection. The blood is not released for processing until the blood tests have come back negative.

The second step is that the plasma is treated in a few different ways to get rid of infection. Depending on the manufacturer, the plasma will get a combination of heat treatment (pasteurisation), addition of solvent detergent, and nano-filtration with or without UV light treatment.

Donor centres and immunoglobulin manufacturers have very high standards for minimising the risk of infection getting into the immunoglobulin supply. Donor centres and manufacturers are inspected regularly and will be closed down if there is any hint of a problem.

A final important safety step is carried out by immunologists, who either do annual hepatitis checks or save a sample of blood for infection testing. You will also be kept on the same immunoglobulin product once you have started. It is through this kind of surveillance that we can be confident that immunoglobulin and its administration are as safe as possible.

What kind of follow-up should I expect if I start immunoglobulin?

The exact protocol for follow-up varies between centres and will also vary depending on your particular situation. You could expect to be seen at least two or three times a year. Sometimes follow-up will be done by a specialist trainee doctor or a specially trained nurse if it is carried out at a recognised teaching centre. You might be asked to bring along the details of your infusions, including the number of batches and possibly a diary of any infections you have had.

You might expect to be assessed from the following points of view:

Is the treatment working?

- Are you still having infections?
- Have you had to have antibiotics, take days off work or even go into hospital?
- Are you getting the correct amount of immunoglobulin (checked by doing a blood test)?
- Are your lungs healthy? You might have breathing tests or a CT scan of your lungs.

Are there any problems?

- Have you had any reactions? What caused them?
- A blood sample may be taken for liver tests and a sample frozen in case it needs testing for infection at a later date.
- You might be offered a technique review if you are on home therapy.

Has anything else changed?

- Have you had any other complications of immune deficiency?
- Are there any new treatments or tests that should be considered?
- Do you still understand why you are on immunoglobulin and what the possible risks are?

At monitoring visits, a huge amount of information will be swapped between you and the immunology team. This can be slightly stressful and it's possible you won't remember everything that has been said. You might want to prepare for the monitoring appointment by checking you have your infusion records and infection diary. A lot of people jot down any questions they think of in the days

leading up to the appointment. You might want to take someone along to the appointment to remember what has been said, or you might just want to take notes.

Why is it important to record the batches of immunoglobulin?

Immunoglobulin is manufactured in batches. Several thousand donations of plasma are pooled in each batch. Very occasionally there are problems with some batches. For example, recently one batch of immunoglobulin caused some people to get an itchy rash. Because it was possible to identify which batch was causing the rash, replacement immunoglobulin could be sent out quickly.

Is it possible I don't need immunoglobulin anymore?

The tests you had before starting immunoglobulin were designed to check whether you would need immunoglobulin for life. However, sometimes immunoglobulin is recommended for people whose immune deficiency may be only temporary. This can happen in small babies or when the immune system has been damaged by medications, for example. It's also possible you were given immunoglobulin for a condition that is no longer regarded as needing immunoglobulin. In these situations there are blood tests that can be done to check how well your immune system is working. If you do stop immunoglobulin, your immunology team will monitor you closely.

What products are available?

There are about half a dozen immunoglobulin manufacturers and the different IVIG and SCIG products available vary slightly. However, each manufacturer must follow international standards on product safety. The blood donor centres and manufacturing plants of all the different companies are inspected from time to time.

How do hospitals ensure they don't run out of immunoglobulin?

In the past, supplies of immunoglobulin from different manufacturers have been withdrawn from time to time. This has happened because, for example, a batch of immunoglobulin has caused a reaction, such as an itchy rash. Another problem is that immunoglobulin is being used to treat many more different diseases, not just immune deficiency. The UK is in a unique position owing to the fact we

do not source national plasma to manufacture immunoglobulin because of the theoretical risk of prion infection. Finally, immunoglobulin costs more in some countries, so manufacturers make a greater profit in different parts of the world.

In the past, there have been occasions when supplies of an immunoglobulin product became very low. People on an affected product had to switch to a different one at very short notice.

For these reasons, the UK Government has taken steps to ensure we have a good supply of immunoglobulin at a national level. These steps include negotiating immunoglobulin prices and supplies with the manufacturer. The Department of Health also runs a scheme to make sure that if a crisis develops, immunoglobulin is reserved for patients who really need it, particularly people with immune deficiency.

What if I want to go on holiday?

Being on immunoglobulin should not affect your holidays. If you are on IVIG, a holiday of up to three weeks could be fitted into your infusion schedule. If you are on weekly SCIG, you will either need to take an infusion with you or have a bigger dose in the weeks before and after your holiday. Your immunology team will help you plan this.

How do I ensure I'm doing home therapy safely?

Your immunology team will be accredited as a home therapy training centre and will not allow you to go on to home therapy until you are safe. You might have to do a short exam! Once you are on immunoglobulin at home, your team will want to do an assessment every so often. Your assessment will happen either at home or at the hospital.

Who can I contact if I want to discuss my treatment?

Your immunology team will give you contact details which you can use if a problem arises at home; for example, if you think you have an infection and you want advice about delaying your immunoglobulin treatment. Some immunology centres offer this service during office hours only. This means you might want to plan your infusions for during the week until you have some confidence. You can also call your immunology centre if you have other concerns that might be to do with immune deficiency.

Your GP, NHS 111 and local emergency department will still be the best people to go to for all other problems; for example, if you had an injury that needed sorting out.

Provision of immunoglobulin within the NHS

In the past, there have been times when the supply of immunoglobulin in the UK has fallen. This has happened if manufacturers have had to stop production for a few months or if manufacturers have got a better price for their product overseas.

Fortunately, these problems do not happen often and they have never stopped patients in the UK getting the immunoglobulin they need. However, immunoglobulin is being used for more and more different illnesses, not just primary immunodeficiencies (PIDs). As a result, solutions to help safeguard supplies for PID patients have been put in place. These include manufacturers 'ring fencing' immunoglobulin especially for PID patients, and NHS systems to ensure immunoglobulin healthcare needs are met. These include clinical guidelines for immunoglobulin use, first implemented in 2008 and revised in 2011, and the Department of Health-initiated National Demand Management Programme for Immunoglobulin.

You can find out more by accessing the guide *Intravenous Immunoglobulin: A Patient Guide to Demand Management* at www.ivig.nhs.uk/documents/ivig_patient_guide.pdf

Clinical guidelines for immunoglobulin use

These ensure best practice in the use of immunoglobulin across all conditions requiring immunoglobulin. You can access and download the clinical guidelines for the different areas of the UK below.

England

Clinical Guidelines for Immunoglobulin Use (May 2008) can be accessed via the PID UK website at www.piduk.org/static/media/up/Clinical_guidelines_for_ig%20use_may2008.pdf and its second edition update of July 2011 at www.piduk.org/static/media/up/Clinical_guidelines_for_ig%20use_updated_july2011.pdf

Northern Ireland

In Northern Ireland immunoglobulin is available as per the Department of Health, Social Services and Public Safety (DHSSPS) guidelines using an evidence-based prescribing process adopted from England's Department of Health guidance. While at present Northern Ireland does not require prescribers to enter individuals onto the demand management national database, this is due to be adopted in due course and will, over time, mean that a clearer picture across England, Scotland and Northern Ireland of the usage of immunoglobulin in PID-specific conditions is gained.

Scotland

Clinical Guidelines for Immunoglobulin Use (second edition update) developed for Scotland can be accessed via the PID UK website at www.piduk.org/static/media/up/Clinical_guidelines_for_ig%20use_scotland_march2012.pdf

Wales

Wales has taken a different approach from the demand management programme in England. A professionally led All Wales Immunoglobulin Strategy Group has been set up. Responsible use of immunoglobulin products is very much a priority and should the lead clinician feel that a particular patient requires immunoglobulin, they would be able to commence treatment. Immunoglobulin products are managed via the Welsh Blood Service and local blood banks.

More questions about immunoglobulin therapy?

Then take a look at this section of our website www.piduk.org/whatarepids/treatment/faqstreatmentofpid

About Primary Immunodeficiency UK

**Primary Immunodeficiency UK
(PID UK) is a national organisation
supporting individuals and families affected
by primary immunodeficiencies (PIDs).**

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

Our website at www.piduk.org provides useful information on a range of conditions and topics, and explains the work we do to ensure the voice of PID patients is heard.

If we can be of any help, please contact us at hello@piduk.org or on **0800 987 8986** where you can leave a message.

Support us by becoming a member of PID UK. It's free and easy to do via our website at www.piduk.org/register or just get in touch with us. Members get monthly bulletins and newsletters twice a year.

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

