

Ig therapy
for adults

Immunoglobulin therapy for adults

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



Supporting families affected
by primary and secondary
immunodeficiency

About this booklet

This booklet provides information on immunoglobulin therapy (Ig therapy). It has been produced by the Immunodeficiency 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 immunodeficiency but should not replace advice from your health team.

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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 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. IVIG is initially given 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 produced exclusively for subcutaneous use by 2005. With SCIG, immunoglobulin is delivered by a needle into the fatty tissues under the skin, where it enters the circulation system 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 40 per cent of people with immune deficiency are on IVIG.

What is in the immunoglobulin?

Immunoglobulin is made from donated blood-derived plasma. During the manufacturing process, 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 that 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, they might try giving you vaccines and checking how well you respond. This 'vaccine challenge' can take several weeks owing to the time lapse between having the vaccines and then the blood tests, and then receiving 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 the immunoglobulin treatment; if you do not benefit, they will suggest stopping it.

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 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, a reaction is most likely to happen when you have just started immunoglobulin.

If you continue to have reactions to immunoglobulin, your immunologist may recommend taking paracetamol or antihistamines first. Sometimes reactions may occur with one batch of immunoglobulin but then 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. Prions have been spread from person to person by blood transfusions but never by immunoglobulin. But because of this theoretical risk, British plasma was not collected for making immunoglobulin until 2021 when the ban was lifted by the Department of Health and Social Care after careful consideration of the evidence on the safety of UK plasma by the Medicines and Healthcare products Regulatory Agency (MHRA).

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. Every time a donor attends the blood centre they are asked a lot of questions, ranging from their sexual activity to any recent travel. They then donate the blood and have 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 to minimise 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. 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 be given breathing tests or a CT scan of your lungs.

Are there any problems?

- Have you had any reactions? If so, 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 appointments, 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 is 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 with you to make 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. 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 occasionally.

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 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. 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 manufacturers. 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 should a problem arise at home; for example, if you think you have an infection and you want advice about delaying your immunoglobulin treatment. Some immunology centres can be contacted 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, an injury that requires treatment.

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 immunodeficiency. As a result, solutions to help safeguard supplies for patients who rely on immunoglobulin and for whom there is no other treatment option, have been put in place. These include the introduction of NHS systems to ensure immunoglobulin healthcare needs are met and the publication of clinical guidelines for immunoglobulin use.

Immunodeficiency UK has a range of other leaflets giving more information on the topic of immunoglobulin. These include:

- Switching immunoglobulin products
- SCIG infusion – a practical guide for patients
- When to give immunoglobulin replacement therapy
- Immunoglobulin replacement therapy: one size doesn't fit all

Clinical guidelines for immunoglobulin use

Clinical guidelines 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

Commissioning Criteria Policy for the use of therapeutic immunoglobulin (Ig) England, 2021 <https://bit.ly/3wckjKP>

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. Northern Ireland enters individuals onto the demand management national database, which helps to provide a clearer picture across England, Scotland and Northern Ireland of the use of immunoglobulin in immunodeficiency conditions that are eligible for treatment with this therapy.

Scotland

Clinical Guidelines for Immunoglobulin Use (third edition update)
<https://bit.ly/3w8XpZQ>

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 and stocks are managed using a national Product Selection Guide. 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.

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About Immunodeficiency UK

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.

Immunodeficiency UK is reliant on voluntary donations. To make a donation, please go to **www.immunodeficiencyuk.org/donate**



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