

Immunoglobulin
therapy

Immunoglobulin therapy

information for parents

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THE

CHILDREN'S HOSPITAL

 **PID UK**
Supporting families affected
by primary immunodeficiencies

About this booklet

This booklet has been produced by the PID UK Medical Advisory Panel and Patient Representative Panel in conjunction with Great Ormond Street Hospital and the Great North Children's Hospital. It provides information on immunoglobulin therapy (Ig therapy) to help answer the questions parents may have about this form of treatment for children and young people affected by primary immunodeficiency (PID). The information should not, however, replace advice from a clinical immunologist.

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Immunoglobulin therapy - information for parents
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What is immunoglobulin replacement therapy?

Immunoglobulin replacement therapy is a blood-based treatment. The immunoglobulin contains IgG antibodies that help to fight infection. Your child has been recommended this treatment because their doctors have found that their immune system is either not making antibodies, not making enough antibodies or the ones they are making don't work properly. Immunoglobulin can be given intravenously (into a vein) or subcutaneously (under the skin).

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 blood via a cannula 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 taking between two and four hours. If your child has side effects with IVIG it is usually because it is being given too quickly. Usually your child will have IVIG treatment in hospital, although in highly selected cases parents or carers can be trained to administer IVIG at home. Most children receiving IVIG in the hospital setting will have their treatment administered in a local hospital, under a 'shared care' agreement with the immunology centre.

Subcutaneous immunoglobulin (SCIG) has been developed more recently than IVIG, with new immunoglobulin preparations being produced exclusively for subcutaneous use since 2005. SCIG is delivered via a needle into the fatty tissue under the skin, from where it enters the blood slowly over a few days. SCIG is usually administered into two separate sites simultaneously, and infusions take approximately 45-60 minutes. 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. Usually families with a child on SCIG learn 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?

The paediatric immunology team will give you all the information you need to help you decide which treatment your child will have. You might want to consider the following factors:

- If your child has really 'bad' veins, then SCIG may be preferable over IVIG.
- If you want to take ownership of your child's illness, then SCIG may be the best choice because home therapy is easier to achieve and manage.
- Weekly SCIG therapy at home may disrupt your family life less.
- If you prefer not to undertake treatments at home, then three-weekly IVIG in hospital may suit your family better.
- Infusion-related side effects are more common with IVIG than SCIG and can be related to the volume and rate of infusion.
- If your child is going to be on immunoglobulin 'long term' (more than six months) or for life, then SCIG will mean less time away from school and fewer hospital visits, plus your child when ready can learn how to prepare their treatment themselves.

Your immunology centre will usually be able to offer either treatment depending on these factors and what suits you and your child best. Often patients start with IVIG and switch to SCIG after good immunoglobulin levels have been achieved, but SCIG can also be started from the outset. Across the UK about 60 per cent of all people with immune deficiency are on IVIG, but the majority of children are on SCIG.

What is in the immunoglobulin?

Immunoglobulin is made from plasma separated out from donated blood. 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 does my child need immunoglobulin?

Immune deficient patients are at a greater risk of infection than others. Clinical trials have shown that for people with antibody deficiency, immunoglobulin treatment results in fewer infections, and the infections that do occur tend to be less serious. There is also evidence that people with antibody deficiency are

more likely to enjoy good health over many years if they receive immunoglobulin correctly. Finally, your child's wellbeing and energy levels are likely to be better if they are on immunoglobulin. Please note that it may take several months before you see these benefits.

What tests does my child need to have before starting immunoglobulin?

Your child's paediatric immunologist will only recommend starting immunoglobulin if your child has had tests which confirm it is the right treatment for them. 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 paediatric immunologist might try repeating your child's vaccinations and checking how well they respond. This 'vaccine challenge' can take several weeks as your child will have to have the vaccines, wait approximately six weeks before a blood test and then get the results.

Your child's paediatric immunologist might suggest your child takes regular antibiotics for a few months to see how well these protect them from infection. This can be done while you are waiting for the results of the vaccine challenge.

Finally, your child's immunologist might suggest your child tries immunoglobulin for a period of time, e.g. a year. If it is clear that your child has benefitted, then the doctor will recommend they continue it, but if your child does not benefit, the immunologist 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. Your child will have their first few infusions in hospital even if you do decide home therapy is your preferred option. This is to minimise the chance of a reaction at home and to allow time to train parents/carers.

Some people get a headache or tummy pain and may feel sick while receiving IVIG. It is also possible to get a headache a day or so after immunoglobulin has been given. Allergic-type reactions that sometimes happen with IVIG or SCIG include rashes, a high temperature, shivering, itching or wheezing.

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 your child has a reaction during an infusion, the first thing to do is to stop the infusion to see if symptoms reduce, then depending on which symptoms have occurred, it may be restarted. Once recovered, the details of the reaction should be recorded in order to inform your child's clinical immunology team. For those on home therapy, this will be covered in the training sessions.

Immunoglobulin is given at a time when there is an infection. If your child has a cold or a chest infection on the day of their infusion, they are more likely to have a reaction. Your child's immunology team will help you recognise the symptoms of infection, so that you can delay their 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 they have just started immunoglobulin.

If your child has reactions when they start immunoglobulin treatment, the chances are that they will gradually reduce and stop after the first few infusions. If your child continues to have reactions with immunoglobulin, their 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 child's immunologist will recommend that the immunoglobulin product is changed because reactions cannot be brought under control. Home therapy can be started six months after any reactions have subsided.

Are there any other safety problems with immunoglobulin?

Immunoglobulin is made from plasma donations. Several thousand plasma 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. Today, 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 infection 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. Owing to this theoretical risk, British plasma is not used for making immunoglobulin.

The other risk is 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 plasma 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, on topics ranging from their sex lives to any recent travel. They then donate the plasma as well as having a series of blood tests to make sure they don't have an infection. The plasma 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 ultraviolet 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. Your child will also be kept on the same immunoglobulin product once they have started, provided that it is well tolerated. It is through this kind of surveillance that we can be confident that immunoglobulin and its administration is as safe as possible.



What kind of follow-up will my child receive if they start immunoglobulin?

The exact protocol for follow-up varies between centres and will also vary depending on your child's particular situation. You can expect to see the immunology team at least two or three times a year. Sometimes follow-up will be done by a specialist trainee doctor if it is a recognised teaching centre. You will be asked to bring along the details of your child's infusions, including the batch numbers and a record of any infections they have had.

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

Is the treatment working?

- Are they still having infections?
- Have they had to have antibiotics, take days off school or even go into hospital?
- Are they getting the correct amount of immunoglobulin (checked by doing a blood test)?
- Are their lungs healthy? They might have breathing tests or a CT scan of their lungs (depending on individual needs).

Are there any problems?

- Have they had any reactions? What caused them?
- A blood sample may be taken for liver function tests and a sample frozen in case it needs testing for infection at a later date.
- You may receive an annual home visit if your child is on home therapy.

Has anything else changed?

- Has your child had any other complications of immune deficiency?
- Are there any new treatments or tests that should be considered?
- Do you (and your child) still understand why they are receiving 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 child's infusion records. 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 batch numbers 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. As it was possible to identify which batch was causing the rash, replacement immunoglobulin could be sent out quickly.

Is it possible my child won't need immunoglobulin anymore?

The tests your child had before starting immunoglobulin were designed to check whether they would need immunoglobulin for life. However, sometimes immunoglobulin is recommended for people whose immune deficiency may be only temporary. This can happen in babies and small children or when the immune system has been damaged by medications. It's also possible your child was 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 child's immune system is working. If your child does stop immunoglobulin, the immunology team will monitor them 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.

What if we want to go on holiday?

Immunoglobulin therapy should not affect your family's holidays. If your child is on IVIG, a holiday of up to three weeks could be fitted into your child's infusion schedule. If they are on weekly SCIG, the schedule could be adapted to allow a break for up to two weeks, or sometimes a single dose of IVIG can be given immediately before the holiday. Your child's immunology specialist nurse will help you plan this.

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

Your child's immunology team will be accredited as a home therapy training centre and you will undergo a training programme in the hospital setting. You will not be allowed to give immunoglobulin at home until you are confident about doing so. You might have to do a short exam! Once your child is on immunoglobulin at home, the specialist nursing team will want to do a review every so often. Your review will happen either at home or at the hospital.

Who can I contact if I want to discuss my child's treatment?

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

Your child's GP, NHS 111 and local emergency department will still be the best people to go to for all other problems, e.g. if your child has had an injury that needs 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 (see www.ivig.nhs.uk/clinicinfo.html).

You can find out more by accessing the guide *Intravenous Immunoglobulin: A Patient Guide to Demand Management* from the website above.

Keeping infusion records (through hospital pharmacies or patient own home therapy records) helps the national immunoglobulin database to be updated so that manufacturers can better manage supply and demand. Importantly these records also mean that any product issues with certain batches of immunoglobulin can be tracked directly to patients. This information is always anonymised.

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 the 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 the PID UK website:

www.piduk.org/whatarepids/treatment/faqstreatmentofpid.

Glossary of terms

allergic reaction – over-reaction of the immune system to a food, environmental substance or drug.

antibody – a type of protein (immunoglobulin) that is produced by certain types of white blood cells. Antibodies fight bacteria, viruses, toxins and other substances foreign to the body.

antihistamine – a type of medicine used to treat allergies, e.g. hay fever.

BSE (bovine spongiform encephalopathy) – commonly known as mad cow disease. In cattle it causes a breakdown of the nervous system. Infection in humans causes the condition variant Creutzfeldt-Jakob disease (vCJD).

cannula – a small plastic tube that is inserted into a vein to give immunoglobulin or other treatments.

clinical nurse specialist – a senior nurse who provides expert advice related to specific conditions or treatment pathways.

CT scan (also known as a CAT scan) – a specialised X-ray that gives pictures of the inside of the body.

deficiency – a lack or shortage.

hepatitis – inflammation of the liver, usually caused by viruses. Hepatitis B and hepatitis C are examples.

HIV (human immunodeficiency virus) – virus infection causing acquired immunodeficiency syndrome (AIDS).

IgG – the most abundant type of antibody present in the body and the main component of immunoglobulin treatment.

immune deficiency – when the immune system's ability to fight infectious disease is compromised or entirely absent.

immune system – the structures and processes that protect the body against infection and disease.

immunoglobulins – proteins (globulins) in the body that act as antibodies. They work to protect against and fight off infections. They are produced by specialist white blood cells (plasma cells / B-cells) and are present in blood serum and other body fluids. There are several different types (IgA, IgE, IgG and IgM), and these have different functions.

infusion – delivery of treatment either into a vein (intravenous) or under the skin (subcutaneous).

intravenous – inside or into a vein; e.g. an immunoglobulin infusion may be given directly into a vein.

IVIG – intravenous immunoglobulin.

nanofiltration – method of removing tiny particles (in this case possible infectious particles) by filtration. Used in the preparation of some brands of immunoglobulin to minimise the risk of transmitting infection.

paediatric immunologist – consultant specialising in the care of children with immunological conditions.

pasteurisation – a process that kills microbes by heating and quickly cooling food and drink, such as milk, juice and canned food. Used in the preparation of some brands of immunoglobulin to minimise the risk of transmitting infection.

plasma – the straw-coloured, liquid part of the blood (that is excluding blood cells). Consists of water containing a large number of dissolved substances, including proteins (including immunoglobulins), salts (especially sodium and potassium chlorides and bicarbonates), food material (glucose, amino acids, fats), hormones and vitamins, and excretory materials.

prion – a small infectious particle that carries no genetic material.

protein – one of the basic building blocks of life. Proteins make up the structure and determine the function of the cells from which all the tissues of our bodies are formed.

SCIG – subcutaneous immunoglobulin.

solvent detergent treatment – a chemical method of inactivating possible viruses during immunoglobulin manufacture.

subcutaneous – 'under the skin'. It also refers to anything relating to the loose cellular tissue beneath the skin; e.g. an immunoglobulin infusion given straight into the tissue directly beneath the skin is said to be given subcutaneously.

variant CJD (vCJD) – a rare and fatal human neurodegenerative condition. The consumption of food of bovine origin contaminated with the agent of bovine spongiform encephalopathy (BSE), a disease of cattle, has been strongly linked to the occurrence of vCJD in humans.

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.

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