Living with an Inhibitor

Your guide to managing hemophilia with inhibitors

National Hemophilia Foundation
for all bleeding disorders

HEMOPHILIA.ORG
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The information contained in this publication is general information only. NHF does not give medical advice or engage in the practice of medicine. NHF under no circumstances recommends particular treatments for specific individuals and in all cases recommends that you consult your physician or local treatment center before pursuing any course of treatment.

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YOU’VE TESTED POSITIVE FOR AN INHIBITOR. NOW WHAT?

Inhibitors are proteins in the blood that inactivate clotting factor. This stops the factor product from working, so bleeding episodes continue. Inhibitors can be treated, but the way they are treated varies from person to person. No two people or situations are the same. Sometimes treatment is similar to that of people with hemophilia who do not have inhibitors. Other times, treatment is more complicated. It depends on such things as how high the inhibitor level (known as the Bethesda titer) is and how the person responds to treatment.

In general, there are three goals for someone with an inhibitor:

- **GOAL ONE:** Treat bleeds
- **GOAL TWO:** Permanently remove the inhibitor
- **GOAL THREE:** Overcome the challenges of inhibitors in your daily life

Inhibitors can cause a whole host of concerns for people with hemophilia, and for families and caregivers. There can be long-term joint damage, as well as social and emotional strain. More is being learned about inhibitors all the time. New treatments are being developed to help people live as healthy lives as possible.

THIS BROCHURE will help you learn about:

- How to treat bleeds when you have an inhibitor
- How your healthcare providers may work toward removing inhibitors from your body
- Ways in which inhibitors can affect your lifestyle
- Tips for how to handle the cost of treatment
- The social and emotional impact of inhibitors

TIP FOR USING THIS BROCHURE:

Not sure what some of the terms mean? Words in orange are explained in more detail in the Glossary at the back.

NEED MORE INFORMATION ON THE BASICS OF WHAT INHIBITORS ARE? Check out NHF’s companion brochure called “Facts About Inhibitors.”
**GOAL ONE: TREAT BLEEDS**

Treatment depends on the type of inhibitor you have: low or high level (titer)

For people with **low-titer inhibitors**, using more frequent and/or higher doses of factor replacement products can often treat bleeds. For people with **high-titer inhibitors**, treating bleeds is more difficult. Increasing the amount of factor is often not an option. These people must be treated with **bypassing agents**.

Clinical research about inhibitors is ongoing, so staying up to date on the latest treatment options is important. A list of treatment products for treating inhibitors is available from NHF’s Medical and Scientific Advisory Council (MASAC) on our website. Visit [www.hemophilia.org/ProductInfo](http://www.hemophilia.org/ProductInfo) for the latest recommendation.

**Bypassing agents**

One way to control bleeds in people with inhibitors is to use bypassing agents. These agents are clotting factors that “bypass,” or go around, the body’s need for factor VIII (8) or factor IX (9), to help clots form.

**THERE ARE TWO MAIN TYPES OF BYPASSING AGENTS:**

1. **Activated prothrombin complex concentrate, or aPCC**
2. **Recombinant activated factor VIIa concentrate**

The US Food and Drug Administration (FDA) has approved each type of medication as treatment for people with inhibitors. These treatments can be very costly (see section below on financial and insurance issues). See MASAC treatment recommendations mentioned above for the names and characteristics of these bypassing agents.
There are two ways that bypassing agents are used:

- As prophylaxis to prevent bleeds
- To treat a bleed that has already begun

There is no standard lab test to show that a bypassing agent is working. Different patients respond differently to the two types of products. However, a patient will know if the medication is working if it is preventing bleeds or if the bleeds resolve quickly after a dose is given.

If the initial dose or type of medication is not working, then the doctor can do one of the following:

- Adjust the dose of the bypassing agent up or down
- Change the type of bypassing agent
- Change how often the bypassing agent is given for prophylaxis
- Add additional medications

Are there drawbacks to bypassing agents?

Although these drugs are very effective, they do have some drawbacks. One drawback is the possible development of a thrombosis, or blood clot. A thrombosis can occur at the site of bleeding or somewhere else in the body. This complication is rare, but in some cases can be very serious and may even be life threatening.

There are several reasons why a person may develop a blood clot. The dosage of bypassing agent may be too high, or it is being administered too frequently. Clots can also form if the person is using both a bypassing agent and oral medications such as aminocaproic acid (Amicar) or tranexamic acid (Lysteda). These two medications prevent clots from breaking down, and should not be used at the same time as a bypassing agent. Occasionally, the use of aPCCs may cause the inhibitor titer to rise. Therefore the HTC physician should draw frequent inhibitor tests to be sure this is not happening.

Plasmapheresis

Plasmapheresis provides a way for doctors to lower the level of an inhibitor (during severe bleeding episodes) enough to allow treatment with factor concentrate. During this process, blood is removed from the body, plasma containing the inhibitor protein is separated from the blood cells and the blood cells are returned to the body. As a result, the inhibitors are removed or reduced to a level where factor can be effective. However, because this is a temporary solution, the body will produce new inhibitors within a few days.
GOAL TWO: PERMANENTLY REMOVE THE INHIBITORS

Treating bleeding episodes is only one aspect of treating people with inhibitors. The second looks at ways to solve the problem of inhibitors themselves.

Immune tolerance induction

For some people, the best option to try to rid the body of inhibitors is immune tolerance induction, or ITI. The goal of ITI is to “teach” the body to accept the clotting factor. In some ways, it is similar to treatments for allergies, by desensitizing the body to the foreign agent. Another way to think about ITI is that it helps the body not see the factor as a threat. When ITI is successful, the body is tricked into thinking factor treatment actually belongs there, and the inhibitor may eventually go away.

ITI is done by giving people increasingly more frequent doses of factor over a given time period. It can take weeks or, in some cases, years until the body gets used to the factor.

There are many different protocols for ITI, which means that not all patients will follow the same treatment plan. For many patients, especially very young children, a port (a surgically inserted device to help give factor through a vein) may be needed to carry out the treatment. It is important to discuss with your doctor how ITI will be given to you or your child. Write down any questions you may have and bring them to your doctor’s appointment.

How well does ITI work?

ITI can work very well, even though it can be a long process. In fact, ITI can remove inhibitors in about 70% of patients with hemophilia A and 30% of those with hemophilia B. For others, ITI can decrease their bleeding complications.

When determining whether ITI is successful, three factors are considered:

1. The inhibitor titer is reduced to less than 0.5 Bethesda units
2. The patient recovers at least 60% of the factor after being given a dose of factor
3. The half-life of factor given to the patient is at least 6 hours

Some patients may not achieve all three but are able to use factor, significantly decreasing the number of bleeding episodes. Decreasing the number of bleeds is the goal for all patients who undergo ITI. Once tolerance is achieved, most patients will continue on some type of prophylaxis.
Which products are used for ITI?

Many patients start ITI using the same factor product they were using when they developed the inhibitor. But many other patients need to switch to a different factor product. Your doctor will discuss products with you and recommend the best one. Remember, everyone is different. What works for one patient may not work for another.

Things to consider if you are thinking about ITI

Be sure to talk to your doctor about the risks and benefits of ITI. If you already go to a hemophilia treatment center (HTC), you may find much support and information from the staff.

The first thing to keep in mind is that ITI is not for everyone. Some people with inhibitors can be treated using other methods discussed in this brochure.

Second, ITI requires a lot of time and resources for clinic visits and treatments. It can disrupt your normal routine, and that of your family or caregivers. And, depending on your progress, the treatment schedule may vary or change from time to time.

Third, a person going through ITI can have setbacks along the way. These include infections and blood clots. To get through these difficulties, you and your family will need dedication and patience.

THE GOOD NEWS IS THAT HELP IS AVAILABLE IF YOU KNOW WHERE TO LOOK FOR IT. Some people rely on their family for support. Others find help through counseling at an HTC. Many people find that both are necessary to go through ITI successfully.
GOAL THREE: OVERCOMING THE CHALLENGES OF INHIBITORS IN YOUR DAILY LIFE

People with inhibitors can live long, fulfilling lives. However, people with inhibitors and their families often face challenges, including those discussed in this section. Finding support and resources to help you and your family through such challenges is key.

Joint and physical activity concerns

Bleeds into joints and muscles can happen in people with hemophilia with or without inhibitors. These types of bleeds are called musculoskeletal bleeds. For people with inhibitors, bleeds are harder to control and take longer to heal. **Below are some of the ways you can deal with these types of bleeds:**

- Being physically active is important to prevent joint and muscle bleeds, and promote good health. Typically, lower-risk activities and sports are advised. But first speak to your healthcare provider, especially your physical therapist, about evaluating any physical activity you’re interested in.

- If you bleed into your joints and muscles when you have an inhibitor, you may need to temporarily use protective gear and/or assistive equipment. These may include crutches, a wheelchair, walker, sling and splints.

- When you have an inhibitor, complete recovery from joint or muscle bleeding is important to reduce your chances of having a repeat bleed in the same joint or muscle. Working with a physical therapist will help you better recover from such a bleed.

- People with inhibitors may experience joint damage from repetitive bleeding, which is an accumulation of bleeding episodes in the same joint, known as a target joint, over time. Joint damage can be treated by surgical and nonsurgical methods.
Financial and insurance coverage considerations

Treatment for hemophilia is costly, even for people without inhibitors. Once an inhibitor develops, treatment can become very expensive. It is important to remember that insurance companies do not always cover all treatment costs. Because of this, patients and their families must consider both the initial costs of treatment and the projected costs of the entire therapy.

People going through inhibitor treatment should be aware that some costs get paid “out of pocket.” And many insurance plans have a limit to how much they will pay for treatment. If you go to an HTC, be sure to talk to a social worker and/or hospital insurance verifier. They can help you work through some of the items listed below. In addition, you can go to hemophilia.org and search for the Personal Health Insurance Toolkit to help assess what your insurance plan will cover.

THINGS TO CONSIDER about the cost or coverage of treatment

- Does your doctor need to provide extra reasons to justify your treatment?
- Will you be treated in a hospital or in an outside office or clinic?
- Does your insurance plan have a special case manager for people with hemophilia?
- Are there programs from the government or drug companies that can help lower your costs?
- Are there costs your insurance will not cover?
Impact of inhibitor treatment

Many treatment plans for inhibitors are intense and long lasting, which can be hard on the whole family. They can cause emotional stress and affect your social life, work and school. Some of the ways you may be affected include:

- You may have to travel long distances to get the care you need
- Some patients develop a fear of needles
- More frequent infusions sometime require use of a port
- Treatment may cause you or your caregivers to be absent from work or school

Social issues for children at school

Treatment can be especially hard on children. They may go through some of the following:

- Limited activities due to intensive therapy
- Social issues from the burden of ongoing treatment
- Fear of needles
- Greater anxiety or depressed moods due to limited physical activity
- More intense desire for independence during teenage years
- Challenges at school from absences for treatment

That’s why support is so important for children. Family members, caregivers, doctors and other health experts can help. Staff at an HTC can help parents with their children’s physical and emotional changes. They can suggest safe activities that meet the needs of each child.

You can also get help completing paperwork, such as developing a 504 Accommodation Plan or an Individualized Education Plan (IEP), and addressing needed accommodations, modifications and support at school.

SOCIAL WORKERS CAN PROVIDE HELP or refer family members to therapists or counselors who can help you with the impact of inhibitors on you, your child and the rest of the family.
Challenges at work

Whether you have an inhibitor yourself or are a caregiver for a child with an inhibitor, the frequent treatment and medical visits can pose challenges at work. The Americans with Disabilities Act (ADA) and Family Medical Leave Act (FMLA) offer protections that may be relevant for you. For instance, they can help you request reasonable accommodations or time off for treatment for you or your child.

What and when you disclose about your bleeding disorder or your child’s in the workplace is a very individual decision. You can find more resources and support from your local NHF chapter, HTC or online at: http://stepsforliving.hemophilia.org/step-out/workplace-issues.

Inhibitors and family dynamics

When someone has an inhibitor, it can truly take a toll on the whole family. Challenges can arise when more time and attention are given to a child or partner with a bleeding disorder. Other issues may surface when asking extended family for support or when educating them on how inhibitors can affect everyone’s lives.

Managing these dynamics can lead to added stress. The social workers at your HTC and local NHF chapters have resources to help navigate these relationships.
DOCTORS AND OTHER HEALTH EXPERTS are learning more about hemophilia and inhibitors all the time.

**INHIBITOR RESEARCH**

In 2015, the results of a large, six-year study were published. The study was called the Hemophilia Inhibitor Research Study (HIRS). It found that people of all ages with hemophilia, not just young children, could get an inhibitor. The study also found that many study participants diagnosed with an inhibitor had no symptoms. These and other findings led to recommendations for testing for inhibitors every year.

New treatments are also being investigated, some specifically for those living with inhibitors. For the most up-to-date treatment options visit hemophilia.org and look for the MASAC Recommendations Concerning Products Licensed for the Treatment of Hemophilia and Other Bleeding Disorders.
**504 Accommodation Plan** is a legal document listing specific accommodations for students with a disability, such as extra time to complete assignments when absent.

**Bethesda titer** is the level or amount of inhibitor in the patient’s blood, measured in Bethesda units (BUs).

**Bypassing agents** are clotting factors used to treat people who have inhibitors. They can “bypass” the need for the deficient clotting factor (VIII or IX), while still helping to form clots to stop bleeds.

**Clotting factor (often called factor)** is a dried powder form of the missing protein; it is mixed with water to become a liquid again before it is administered. Some clotting factor products, called plasma-derived factor, are made from donated human blood plasma. Others, called recombinant clotting factor products, are genetically engineered in a laboratory and do not use human blood proteins.

**High-titer inhibitor** means your body has a strong response against the clotting factor. Your test results are more than 5 Bethesda units (5 BUs).

**Immune tolerance induction (ITI)** is a type of treatment for people who have inhibitors. The goal of ITI is to rid the body of inhibitors. It involves giving many doses of factor VIII or IX products over many months to train the immune system to stop making inhibitors and accept, or tolerate, the treatment.

**Individual Education Plan (IEP)** is a plan created to ensure that a child who has a disability identified under the law and is attending an elementary or secondary educational institution receives specialized instruction and related services, including necessary modifications.

**Low-titer inhibitor** means your body has a low response against the clotting factor. Your test results are less than 5 Bethesda units (5 BUs).

**Plasmapheresis** is the process used to separate inhibitors in the plasma from blood cells and other components in a patient’s blood.

**Port(s)** are devices that are surgically placed in the body to make it easier to administer clotting factor products into the bloodstream. Some of them are inserted under the skin in the chest. Your doctor will help you decide which type is best for you or your child.

**Prophylaxis** is the administration of clotting factor on a regular schedule to prevent bleeding.

**Thrombosis** is a clot that forms in an artery or vein in the body. It may occur spontaneously or following treatment with aPCCs.
WANT TO KNOW MORE ABOUT LIVING WITH INHIBITORS?

The National Hemophilia Foundation is your source for information on all bleeding disorders. **On our website, hemophilia.org, you can:**

- Find a hemophilia treatment center (HTC) or NHF chapter near you
- Get information on our online and in-person inhibitor education programs
- Learn what the latest recommendations are for treatment
- Access tools to advocate for you and your family for healthcare coverage

At stepsforliving.hemophilia.org, you can also find interactive information, videos and tools for living with a bleeding disorder, including an inhibitor, at any life stage.

YOU ARE NOT ALONE

The community of healthcare professionals and people with bleeding disorders can help you. Families, friends and loved ones often come together in groups to support each other. During NHF’s Inhibitor Education Summits people who have (or had) inhibitors and their caregivers can meet. Many form strong bonds that last a lifetime.
NOTES/QUESTIONS FOR YOUR HEALTHCARE PROVIDER:
The National Hemophilia Foundation (NHF) is dedicated to finding better treatments and cures for inheritable bleeding disorders and to preventing the complications of these disorders through education, advocacy and research. Established in 1948, the National Hemophilia Foundation has chapters throughout the country. Its programs and initiatives are made possible through the generosity of individuals, corporations and foundations as well as through a cooperative agreement with the Centers for Disease Control and Prevention (CDC).