WFH
WORLD FEDERATION OF HEMOPHILIA
FÉDÉRATION MONDIALE DE L'HÉMOPHILE
FEDERACIÓN MUNDIAL DE HEMOFILIA

What is **Prophylaxis?**

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Content

What is **Prophylaxis?**

Prophylaxis is the regular administration (intravenously, subcutaneously, or otherwise) of a hemostatic agent with the goal of preventing bleeding (especially life threatening or recurring joint bleeding) in people with hemophilia. The goal of prophylaxis is for people with hemophilia to lead active lives, and to achieve quality of life that is comparable to non-hemophilic individuals.

Prophylaxis should be the standard of care everywhere in the world. The clinical recommendation of prophylaxis comes from the scientific observation of patient data that people with moderate or mild hemophilia (who have clotting factor levels at 1% or above) experience far less spontaneous bleeding. They have less joint damage than people who have severe hemophilia (who have less than 1% clotting factor) and an improved quality of life.

DID YOU KNOW?

The most common long-term complication of hemophilia is joint disease.

Why is Prophylaxis Recommended?

Unlike on-demand therapy, which is a *reactive* response to stopping a bleed that is in progress, prophylaxis is given to *prevent* bleeding before it starts. On-demand therapy may reduce the pain and debilitating impact of individual bleeds, but it cannot significantly alter the bleeding profile.

Therefore, on-demand therapy does not change the natural progression of hemophilic arthropathy, which leads to musculoskeletal damage and other complications caused by bleeding. The use of prophylaxis is always recommended and preferred over on-demand therapy, as the ideal is for people with hemophilia to not experience any bleeds (i.e., achieve "zero" bleeds), as each bleed can cause damage, especially in the joints.

Studies on prophylaxis show that:

- Keeping minimum factor levels above 1% with regular infusions of clotting factor concentrates (CFCs) reduces the risk of bleeding and prevents joint damage.
- Children and adults who receive prophylaxis experience fewer bleeds and consequentially have healthier joints.

Doctors recommend that people with hemophilia A or B who have a severe bleeding profile should be on prophylaxis sufficient to prevent bleeds at all times. This should be individualized, taking into consideration:

- Bleeding patterns
- Status of joints
- How the individual's body uses the hemostatic agent
- Personal preference and assessment of the effectiveness of prophylaxis

DID YOU KNOW?

Prophylaxis will not help repair joints that are already damaged.

However, it will decrease the frequency of bleeding, may slow progression of joint disease, and may improve quality of life.

What Are the Types of Prophylaxis?

There are several types of prophylaxis, defined according to when prophylaxis starts.

CONTINUOUS PROPHYLAXIS

is given regularly over a period of several months and often years:

Primary prophylaxis
is started before any joint disease is documented, and before the second joint bleed. Usually started in children aged three years and younger.

Secondary prophylaxis
is started after two or more joint bleeds (but before joint disease). Usually started in children aged three years and older.

Tertiary prophylaxis
is started after joint disease is diagnosed.

INTERMITTENT OR PERIODIC PROPHYLAXIS

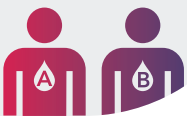
is given for shorter periods of time, usually a few weeks or months, such as after surgery or for physiotherapy/rehabilitation.

For young people with severe hemophilia A or B, starting prophylaxis before the age of 3 is ideal to prevent joint disease. Starting prophylaxis in adolescents and adults with hemophilia who have joint damage is still recommended, as it will reduce joint bleeds and spontaneous and breakthrough bleeding and slow the progression of joint disease.

Adapted from recommendation 6.1.2 and 6.1.3 of the WFH Treatment Guidelines for the Management of Hemophilia, 3rd edition

In countries with healthcare constraints, prophylaxis is still recommended over episodic factor therapy for patients with severe hemophilia A or B, even when the only option is to use lower factor doses. This will still reduce joint bleeds and other spontaneous and breakthrough bleeding, and better preserve joints.

Adapted from recommendation 6.10.1 of the WFH Treatment Guidelines for the Management of Hemophilia, 3rd edition



What Do We Give for Prophylaxis?

Prophylaxis treatment options now include standard half-life (SHL) and extended half-life (EHL) replacement therapy and non-factor replacement therapy. As of publishing this booklet, only one non-factor replacement therapy is available for people with hemophilia A, while SHL and EHL CFCs are available for people with hemophilia A or B.

REGULAR REPLACEMENT THERAPY

Prophylaxis with SHL and EHL CFCs is referred to as **regular replacement therapy**. It involves the regular infusion of the missing clotting factors with the aim of raising the levels such that bleeding stops (FVIII for people with hemophilia A, and FIX for people with hemophilia B).

Prophylaxis with regular infusion of CFC attempts to raise clotting factor levels and to always keep them at 1% or higher. Different dosing regimens (high-, intermediate-, or low-dose), using either SHL or EHL CFCs, are used to achieve this. People with hemophilia should consult with their local physician or Hemophilia Treatment Centre (HTC) as part of their treatment plan.

A prophylaxis treatment plan and schedule using CFCs should include the following:

- The type of factor product to be used
- The dose (how much) of factor administered with each infusion
- The frequency (how often) at which the factor is administered
- The time (of day or week) that factor is administered

EXTENDED HALF-LIFE REPLACEMENT THERAPY

EHL CFCs have been designed to maintain factor levels for a longer period in the blood. Overall, EHL CFCs allow people with hemophilia to:

1. **Reduce the number of infusions needed** to maintain the levels of protection similar to SHL CFCs, resulting in better adherence and more people starting prophylaxis. This includes:
   - Fewer clinic visits or home care nurse visits, especially when starting prophylaxis, and less treatment burden for caregivers and affected individuals
   - Less need for central venous access devices, resulting in reduced morbidity and cost savings
   - Less burdensome dosing schedules, meaning less infusions in the morning or on work/school days
2. **Increase their factor levels** for longer and achieve higher levels of bleed protection with fewer infusions than SHL, which may lead to improved quality of life, such as increased participation in sports without the increased risk of bleeding.

TAILORED PROPHYLAXIS FOR SHL AND EHL REPLACEMENT THERAPY

Tailored prophylaxis regimens are individualized to the needs of each person: people with hemophilia get a prophylaxis regimen based to their own needs. Prophylactic regimens should also be flexible enough to change with time as the individual's circumstances change; if people with hemophilia continue to experience bleeds, their prophylaxis regimen should be increased (in dose, frequency, replacement therapy or any combination) to prevent bleeding.

An effective, tailored, prophylaxis protocol considers the following:

- Age
- Weight
- Bleeding pattern and phenotype
- Joint health
- Level and timing of physical activity you engage in
- Clotting factor levels
- Ability to adhere to a prophylaxis protocol
- Venous access
- Personal preference

NON-FACTOR REPLACEMENT THERAPY

Non-factor replacement therapies use other mechanisms to allow the body to stop bleeding due to deficient clotting factors in people with hemophilia. At the time of publication (2021), only one product (emicizumab) is available and licensed as non-factor replacement therapy for Factor VIII, including those with hemophilia A who have an inhibitor. Other therapies are currently in clinical trials and may come to market over the next few years.

Emicizumab does not replace the missing Factor VIII in people with hemophilia A, instead it mimics FVIII's function so that the clotting process can proceed.

Emicizumab can only be used as prophylaxis in people with hemophilia A. It is not used to treat acute bleeding episodes.

Thus, CFCs will still be required for treatment of acute bleeding.

Other benefits of emicizumab include:

- Subcutaneous route of administration (i.e., injection under the skin)
- Stays in the body longer, and can be administered as infrequently as once per week, or every 2 or 4 weeks (Please consult full prescribing instructions or your HTC for detailed information on dosage)
- Prophylaxis regimens are less burdensome due to decreased frequency of infusions, which can lead to increased adoption of, and adherence to, prophylaxis

CAUTION: While on emicizumab, people with hemophilia who have inhibitors should **not** be given activated prothrombin complex concentrate (aPCC) to treat breakthrough-bleeding episodes, as this may result in a clotting thrombotic event. (Please consult the HTC and risk management guidance for more information.)

When Do You START Prophylaxis?

The best approach is to start prophylaxis as early as possible, to preserve joint health and prevent joint disease. Where access to CFCs is limited, lower doses are an effective option.

Subcutaneous treatment can address the challenges of accessing veins. This may allow prophylaxis to be started at a much earlier age, and may reduce the risk of bleeding that occurs in very young children (<12 months), before traditional prophylaxis usually begins. As of publication (2021), studies are ongoing to determine the safety of emicizumab in this age group.

When Do You STOP Prophylaxis?

A person with hemophilia who continues to benefit from effective prophylaxis (which means having less bleeding episodes, better joint health, and improved quality of life), should continue with prophylaxis indefinitely.

This is a recommendation commonly shared by the World Health Organization, the World Federation of Hemophilia, and many other international and national organizations involved with hemophilia care.

For patients with severe hemophilia A or B, especially children, the standard of care is regular long-term prophylaxis. This will help prevent joint bleeds, spontaneous and breakthrough bleeds, maintain musculoskeletal health, and promote quality of life.

Adapted from recommendation 6.2.1 of the WFH Treatment Guidelines for the Management of Hemophilia, 3rd edition

Source: WFH Guidelines for the Management of Hemophilia, 3rd edition (2020). For more detailed information about prophylaxis, please refer to the guidelines at https://elearning.wfh.org/resource/treatment-guidelines/

Prophylaxis Dos and Don'ts

DOs	DON'Ts
If you (or your child) are not yet on prophylaxis, talk to your doctor or health care team about starting.	Think it is too late to begin prophylaxis – although prophylaxis cannot reverse joint damage, it may slow the progression, improve quality of life, and decrease frequency of bleeding.
Start prophylaxis as early as possible.	Skip or postpone your treatment schedule.
Advocate for individualized, or tailored, prophylaxis.	Expect prophylaxis to reverse joint damage.
Follow the dosage schedule that is given to you by your doctor or health care team.	Wait for your next appointment if you have an adverse reaction or bleeding – see your doctor immediately.
If you experience an adverse event while on prophylaxis, see your doctor immediately; this includes bleeds.	Ignore break-through bleeds, especially recurring in the same joint, as they may lead to a target joint.
Talk to your health care team about the possibility of home therapy or shared care with local health care providers.	
Have regular checkups with your HTC to review your prophylaxis treatment plan.	
Keep track of your treatment in a logbook including any adverse events (see next page for more details).	
If prophylaxis isn't working for you, see your doctor.	

Prophylaxis Logbook

It is important to record the following information when you receive prophylaxis, so that your doctor can follow-up with you and make sure you are on the right treatment for you as an individual.

There are many ways to keep track of bleeding episodes and treatments:

1. **Your own logbook:** This can be by way of a hard copy log-book or an electronic record; what is important is that your record should include:
   - **a.** Date of the infusion/administration
   - **b.** On-demand treatment (site of the bleed)
   - **c.** Prophylaxis (site of the bleed should a breakthrough bleed occur)
   - **d.** Name of the product
   - **e.** Amount infused in IUs (International Units) or mg
   - **f.** Lot number
   - **g.** Adverse reactions

Please check with your HTC if they have a preferred method. **See next page for a printable logbook.**

2. **myWBDR** – If your HTC is part of the World Bleeding Disorders Registry, you can use the mobile application on your smart phone to track your prophylaxis treatment and any bleeding events.

   Application available for download here :

iOS **Android**

TREATMENT LOGBOOK

Name of Patient		Missing Factor Type				
		Inhibitor Status				

Date of Infusion/ Administration	Name of Product	Amount Infused (IU) / mg	Lot Number of Product	Expiration Date	Any Adverse Reactions?	Indication for Infusion*

*Prophylactic dose infusion, acute bleeding episode (including location of bleed), etc.

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