SDM
WFH SHARED DECISION MAKING TOOL

CLOTTING FACTOR REPLACEMENT THERAPIES

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What is clotting factor replacement therapy?

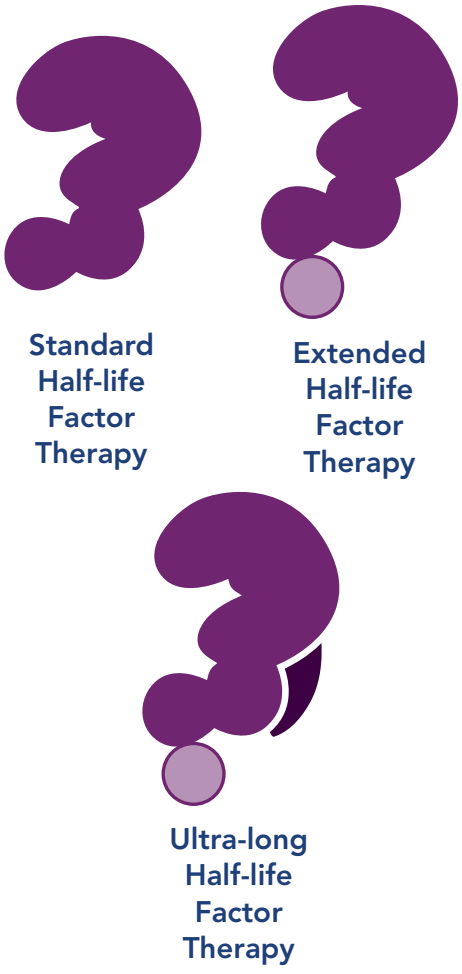
Clotting factor replacement therapies are a prophylactic treatment for hemophilia A and hemophilia B. Clotting factor replacement therapies provide the missing factor VIII or factor IX, allowing the blood to clot efficiently. These therapies can also be used for on-demand treatment.

Clotting factor replacement therapies provide a short-term increase in factor levels by injecting the needed clotting factor protein. The body does not produce this replacement factor; therefore, the effects are temporary, and injections must be administered regularly to maintain effective clotting factor levels and prevent bleeds (prophylaxis) or as needed to stop bleeds (on-demand). The recommended frequency of administration for prophylaxis varies between products.

What are the different types of replacement therapies?

The three clotting factor replacement therapy types are standard half-life (SHL), extended half-life (EHL), and ultra-long half-life (UHL; hemophilia A only). After injecting clotting factor replacement therapy, your factor levels increase immediately but decrease over the next few days. Half-life refers to how long it takes for the replacement clotting factor to decrease by half inside your body.

Many different SHL and EHL medications are available for both hemophilia A and hemophilia B. The most recent clotting factor replacement therapy for hemophilia A is a UHL, efanesoctocog alfa, which has a 3- to 4-fold longer half-life compared to other FVIII clotting factor replacement therapies and therefore requires less frequent treatment.[1] This longer half-life provides mild-to-normal factor VIII activity between treatments and is sometimes referred to as "high sustained factor" (HSF) therapy.



How is the mechanism of action for clotting factor replacement therapies different from other treatments for hemophilia?	The main treatment types for hemophilia are clotting factor replacement therapy, bispecific antibodies, re-balancing agents, and gene therapy. All these treatments help the blood clot more efficiently, but they all work in different ways. Clotting factor replacement therapies temporarily increase factor levels by injecting the needed clotting factor protein directly into the blood of a person with hemophilia. Bispecific antibodies are Y-shaped proteins that act as a bridge between factor IXa and factor X, which helps the blood to clot more efficiently. This antibody bridge mimics the function of the missing activated factor VIII (i.e., factor VIIIa-mimetic). Rebalancing therapies restore the disrupted balance between the levels of anticoagulation (i.e., anti-clotting) factors and clotting factors in the blood, thereby improving blood clotting. Gene therapy introduces a working copy of the missing clotting factor gene. Once the gene is introduced, the body can produce the missing protein and maintain adequate clotting factor levels, on its own, for an extended time.

TREATMENT WITH CLOTTING FACTOR REPLACEMENT THERAPIES

Who is eligible to use clotting factor replacement therapies?	Adults and children with hemophilia A or B who do not have inhibitors are eligible for clotting factor replacement therapy.[1]
How are prophylactic clotting factor replacement therapies administered?	Clotting factor replacement therapies are administered through an injection into your vein. The injection usually takes 5–10 minutes and can be done at home or a clinic.
What is the treatment frequency for prophylaxis with clotting factor replacement therapy?	Prophylactic treatment with clotting factor replacement therapies aims to maintain enough clotting factor levels to prevent bleeding. The frequency and dosage of the infusion are dependent on the individual's specific needs, hemophilia severity, and the type of factor replacement product being used. Clotting factor replacement therapy must be injected regularly to keep factor levels high and prevent bleeding. In hemophilia A, SHL therapy is typically administered 2–4 times weekly, EHL therapy is typically administered twice weekly, and UHL therapy is administered once weekly.[1] In hemophilia B, SHL and EHL therapy are typically administered 1–2 times weekly.
Can clotting factor replacement therapies be used in combination with other hemophilia treatments?	Yes. Clotting factor replacement therapies can be used in combination with other hemophilia treatments.[1]

EFFICACY OF CLOTTING FACTOR REPLACEMENT THERAPIES

How will clotting factor levels be affected?	Clotting factor levels will increase immediately after treatment, decrease rapidly, and return to baseline within days without repeat treatment. The rapid decrease in factor levels necessitates regular treatment to keep factor levels high. The time that it takes the replacement clotting factor to decrease by half is called the "half-life." EHL and UHL replacement therapies remain in the blood longer, and therefore, require less frequent dosing to maintain adequate factor levels.[1] UHL therapies have been shown to maintain near-normal factor levels for four days after treatment.
How will clotting factor replacement therapies affect my annual bleed rate?	Any form of regular prophylactic treatment is likely to reduce your annual bleed rate. Annual bleed rate is calculated as the sum of all bleeds experienced over a 12-month period and is highly dependent on individual factors such as age, prior bleeding history, physical activity, lifestyle, dosing regimen, and adherence to the dosing regimen. It is typically presented as an average (i.e., mean) or median (the middle value within the dataset). In clinical trials in adults with hemophilia, the median annual bleed rates with SHL clotting factor therapies range from 0–2 for hemophilia A and 1–2 for hemophilia B.[1] The reported median annual bleed rates with EHL clotting factor therapies range from 1–2 for hemophilia A and for hemophilia B.[1] The UHL clotting factor therapy, efanesoctocog alfa, is only available for hemophilia A and the reported median annual bleed rate is 0; 55% of patients experienced zero bleeds and 64% of patients experienced zero treated bleeds.[1]

SAFETY OF CLOTTING FACTOR REPLACEMENT THERAPIES

What are the potential side effects of clotting factor replacement therapies?	The most common side effects of clotting factor replacement therapies include injection site reactions and allergic reactions. The reported side effects vary by medication.
Are there any known serious side effects or risks?	One of the most significant side effects associated with clotting factor replacement therapy is the potential for the development of inhibitors, which are antibodies that can bind to and neutralize the replacement clotting factors. Inhibitors can reduce the effectiveness of treatment and increase the risk of bleeding. If inhibitors are going to occur, they typically develop within the first 75 days of exposure. Inhibitors occur in approximately 20–30% of previously untreated people with hemophilia A and 3–5% of previously untreated people with hemophilia B.[2] The rate of inhibitor development following UHL therapy is unknown.

Last reviewed: July 2023
This is a living document that will be updated as new evidence becomes available.

MONITORING AND FOLLOW-UP AFTER CLOTTING FACTOR REPLACEMENT THERAPY TREATMENT

How often will you need follow-up and monitoring with clotting factor replacement therapies?	As with all hemophilia treatment classes, regular monitoring by your healthcare team is recommended. Clinical review should be conducted annually and as needed.
What will happen in the event of a bleed, injury or surgery?	Your healthcare team will work with you to develop a personalized plan for managing any bleeds, injuries, or surgeries while taking clotting factor replacement therapies for prophylaxis. This is likely to include additional doses of clotting factor, additional medications, and/or physical therapy to manage bleeding and pain. If you need to have surgery your healthcare team will carefully manage your treatment to ensure that you have enough clotting factor for the procedure. This may involve increasing your dose of clotting factor replacement therapy before and after the surgery.

CLOTTING FACTOR REPLACEMENT THERAPY TREATMENT IN CHILDREN AND ADOLESCENTS

Are clotting factor replacement therapies approved for use in children and adolescents?	Yes. The majority of SHL, EHL, and UHL clotting factor medications are approved for prophylactic and on-demand use in infants, children, and adolescents.
Are there any special considerations for treating children with clotting factor replacement therapies?	Infants, children, and adolescents tend to the clear the drug from their body faster. Therefore, for many SHL and EHL medications children and adolescents may require either an increased treatment dosage or an increased frequency of treatment. This should be discussed with your healthcare team. Pediatric treatment with the UHL, efanesoctocog alfa, does not require dose or frequency adjustment in younger patients.

1 Prescribing information from approved SHL, EHL, and UHL products from the FDA and EMA.
2 Srivastava, A, Santagostino, E, Dougall, A, et al. *WFH Guidelines for the Management of Hemophilia*, 3rd edition. Haemophilia. 2020: 26(Suppl 6): 1–158.

Last reviewed: March 2024
This is a living document that will be updated with new evidence twice per calendar year. The cutoff dates are June 30 and December 31, with updates taking place in the following month(s). Any new evidence after these cutoffs will be included in the next update.