Irish Haemophilia Society

Emicizumab (Hemlibra®)

For People With Factor VIII Deficiency Without Inhibitors

Contents

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This publication is produced by the Irish Haemophilia Society as an educational tool for members. The I.H.S. does not engage in medical practice and does not recommend particular treatment for specific individuals. It is strongly recommended that individuals seek the advice of their haemophilia treating clinician and / or consult printed instructions provided by the pharmaceutical company before administering the therapy referred to in this publication. The I.H.S. does not endorse particular treatment products or manufacturers.

Emicizumab (Hemlibra®) - for people with Factor VIII deficiency without Inhibitors

This booklet is about Emicizumab (Hemlibra®), one of the latest treatments for people with severe haemophilia A (congenital factor VIII deficiency, FVIII < 1%) without factor VIII inhibitors.

What is Emicizumab (Hemlibra®)?

Hemlibra® is a bi-specific monoclonal antibody. A monoclonal antibody is a type of protein made in a laboratory that can bind to substances in the body. Normally, a monoclonal antibody is made so that it binds to only one substance. A bi-specific monoclonal antibody is one that is made to bind specifically to two substances - in this case Factor IXa (9) and Factor X (10). This is not a factor protein. Hemlibra® is licensed for prophylactic treatment only and can NOT be used to treat acute bleeding episodes.

Who can use Hemlibra®?

Hemlibra® is a treatment for anyone with

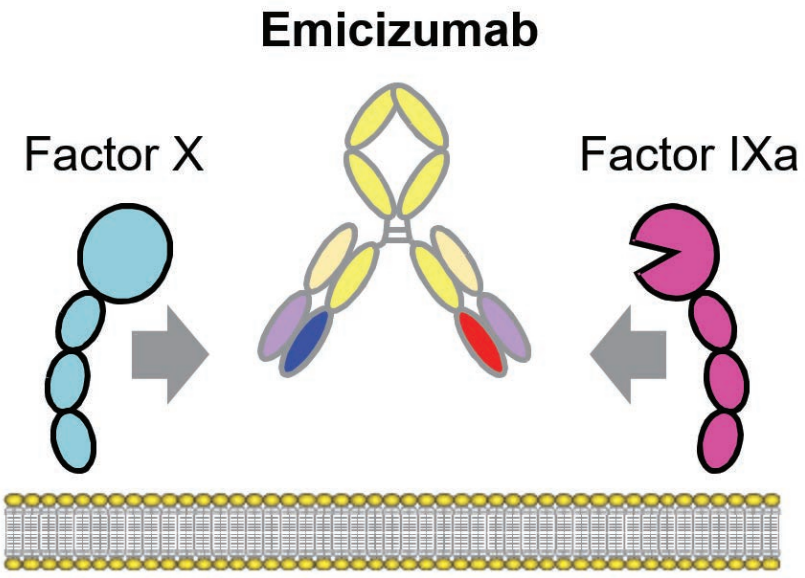
- Severe haemophilia A (FVIII deficiency) without inhibitors
- Haemophilia A (FVIII deficiency) of any severity with Inhibitors (see separate booklet)

Is Hemlibra® suitable for children?

Hemlibra® was used in clinical trials in infants, children and adolescents. No difference in dose or side effects was reported in younger age groups. In children less than one year of age, the blood system is still developing. If your child is less than one year old, your doctor may prescribe Hemlibra® only after carefully weighing the expected benefits and risks of using this product.

How does Hemlibra® work?

When you infuse FVIII, you are replacing the FVIII that is missing from the body. FVIII connects two other proteins activated FIX (FIXa) and FX protein. FVIII creates the bridge between these proteins so the clotting process continues to form a clot and stop bleeding. Instead of the FVIII protein bridging the other two proteins, it is the antibody that does this connection. So Hemlibra® is said to copy or "mimic" the action of FVIII and hence is called a "mimetic" treatment.



Is the half-life of Hemlibra® different from FVIII?

The half-life means how long it takes for FVIII to be reduced by half in your body. With FVIII, the half-life of FVIII concentrates can range from 8-22 hours depending on your body's response and the product that you are using. This is why FVIII treatments are given frequently so that you maintain the level of protection in your blood to prevent bleeding. The half-life of Hemlibra® is 646 hours - or about 4 weeks.

How much Hemlibra® should I use?

The dose of Hemlibra® depends on your weight and your doctor will calculate the amount (in mg) and corresponding amount of Hemlibra® solution (in mL) to be injected.

When you first start taking Hemlibra you need to take four once weekly doses, we refer to this as the "loading dose". This allows the Hemlibra® to build up in your body. During the first week of starting Hemlibra® you may need to continue on your current prophylaxis treatment to prevent any bleeding which may occur while the Hemlibra® levels are building up in your body.

The loading doses are taken on weeks 1 to 4. The dose is 3 milligrams for every 1 kilogram you weigh and given as a once weekly injection.

Your first maintenance dose must be given on Week 5. There are three different maintenance doses available to you; weekly, fortnightly or monthly. The dose of Hemlibra® is different for each frequency. The decision as to which frequency is right for you, will be made by you and your doctor.

- Once weekly - 1.5 milligram for every 1 kilogram you weigh (1.5mg/kg)
- Every two weeks - 3 milligrams for every 1 kilogram you weigh (3mg/kg)
- Every four weeks - 6 milligrams for every 1 kilogram you weigh (6mg/kg)

Hemlibra® is currently available in four different vial sizes:

- 30mg/1ml
- 60mg/0.4ml
- 105mg/0.7ml
- 150mg/1ml

Different Hemlibra® concentrations (30 mg/mL and 150 mg/mL) should not be combined in a single injection when making up the total volume to be injected. The amount of Hemlibra® solution given in each injection must not be more than 2 ml. If your total volume is greater than 2ml you will need to give two injections per dose or you may decide to look at a different maintenance frequency to avoid two injections.

The number of vials and the number of injections required per Hemlibra® dose will vary depending on your body weight and the maintenance frequency. These options will be discussed with you should you decide to switch to Hemlibra® .

How is Hemlibra® given?

Hemlibra® is given as an injection under the skin (a subcutaneous injection), so you do not need to access a vein. The recommended places to give an injection are:

- the front of the waist (lower abdomen), at least 5cm away from the navel
- the upper outer arms (only suitable if given by caregiver), or
- the front of the thighs.

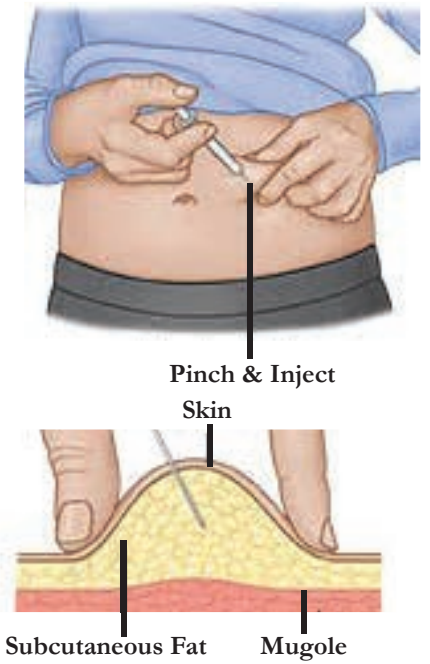
Use only recommended places for injection.

- For each injection, use a different area of the body to the one you used last time.
- Do not give injections where the skin is red, bruised, tender, hard, or areas where there are moles or scars.
- When using Hemlibra®, any other medicine injected under the skin should be given in a different area.
- Injection site irritation or redness can occur.
- Your haemophilia nursing team will train you on how to inject your Hemlibra®.

What if I miss a dose?

If you miss a treatment on your scheduled day, you should take the treatment as soon as you remember, then continue with your normal schedule. You must not take two doses of Hemlibra® on the same day. If you have forgotten to take your treatment and are unsure what to do, you should contact your treatment centre for advice.

Subcutaneous Injection



Do I still need Factor VIII?

Hemlibra® is a prophylactic treatment only and cannot be used to treat a bleed or for surgery. This means that if you have a bleed you may need to get FVIII. You should contact your treatment centre if you have a bleed and they will give you FVIII concentrate or treatment advice of how best to treat your bleed.

What is my factor level on Hemlibra®?

This is not known exactly but the protection against spontaneous bleeds appears to be similar to a person with mild FVIII deficiency with a FVIII level of about 10%. Treatment with Hemlibra® does not normalise the blood clotting system and additional treatment with FVIII or FVIII concentrate may be needed if bleeding or an injury occurs or if a surgical or dental procedure is needed.

Does Hemlibra® cause factor VIII inhibitors?

Hemlibra® is not a factor VIII protein. When your body develops an inhibitor to FVIII, it creates an inhibitor (also an antibody) that recognises and then attaches itself to the FVIII protein to stop it doing what it is supposed to do. As your body has built the inhibitor to specifically recognise and search for FVIII proteins, the inhibitors don't recognise the Hemlibra® antibody and therefore let it carry on to do its job.

Will I ever get an FVIII inhibitor?

FVIII inhibitors usually occur within the first 50 injections (also known as exposure days) of FVIII. If you have received Hemlibra® after then, it is unlikely that you will develop an inhibitor. If you receive Hemlibra® before you receive 50 FVIII injections, there is a possibility that you still might develop an inhibitor to FVIII in the future. It may be suggested that you receive at least 50 injections of FVIII before starting or while using Hemlibra in order to tolerise you against the risk of developing an inhibitor to FVIII.

Can my immune system react to Hemlibra®?

Yes. Your body identifies the Hemlibra® as a foreign body and creates an antibody, known as anti-drug antibodies (ADAs). There are two types of ADAs. A neutralising and a non-neutralising ADA. A non-neutralising anti-body will attach itself to the Hemlibra® but will not stop it building the bridge between FIXa and FX and therefore the Hemlibra® continues to work. A neutralising antibody stops the Hemlibra® working completely. In trials, ADAs were present in 3.5% of people but <1% of these were neutralizing. A neutralising ADA may be suspected if you start to develop spontaneous bleeding and blood tests can be done to see if an ADA has developed.

What are the benefits of Hemlibra®?

- There is a consistent level of protection from bleeding.
- You will have fewer injections.
- You will dramatically reduce the need for intravenous injections.
- Subcutaneous injections (which might take some getting used to) are easier to give than Intravenous therapy.
- For minor surgeries such as some dental treatment or other invasive procedures

you may not need additional FVIII or you may require only Tranexamic Acid if you do have some bleeding. You should always check with your haemophilia centre prior to having any procedure carried out, especially if it is being carried out in a facility or hospital which is not your Comprehensive Care Centre.
- Trials have shown that the steady state of protection has been shown to reduce bleeding events over time.
- The risk of developing antibodies to Hemlibra® which prevent it from working is very low.

What are drawbacks to Hemlibra® treatment?

- Hemlibra® offers a different type of protection to the current FVIII treatment. Hemlibra® gives you a constant level of protection which is higher than the trough (lowest level) currently achieved with FVIII prophylaxis but it also never provides the higher level of protection in the normal clotting range that you get with FVIII treatment in the hours immediately following a FVIII injection. If you are an individual who is very active or possibly involved in some sports, Hemlibra® may not be for you. You should discuss this with your treatment centre to decide currently which is the best treatment option for you.
- It cannot be used to treat a bleed, so you need to continue to use FVIII concentrate to treat any bleeding episode
- Routine clotting/coagulation blood tests may be misleading in people on Hemlibra®. This is important in cases of emergency if you are unable to tell the treating clinicians you have haemophilia.
- Hemlibra® takes up to 6 months to leave your system if you stop taking it.
- It is a newer treatment; all the possible benefits and risks may not be yet be known.

What should I know about Hemlibra® safety and side effects?

Like all medicines, this medicine can cause side effects, although not in everybody who uses the medicine.

Side effects

Very common: may affect more than 1 in 10 people

- A reaction in the area where the injection is given (redness, itching, pain). To avoid injection reactions, change the site of injection and try not to give two injections in a row in the same place.
- Headache
- Joint pain

Common: may affect up to 1 in 10 people

- Fever
- Muscle aches
- Diarrhoea

Uncommon: may affect up to 1 in 100 people

- Destruction of red blood cells, which create a type of clot that occurs in small blood vessels that may cause harm to your kidneys, brain, and other organs. These are known as thrombotic microangiopathy.
- Blood clot in a vein behind your eye (cavernous sinus thrombosis)
- Severe damage of the skin tissue (skin necrosis)
- Blood clot in a vein near the surface of the skin (superficial thrombophlebitis)

If you experience any of these symptoms during or after treatment with Hemlibra®, get medical help right away.

How is Hemlibra® stored?

Hemlibra must be kept in its original box and stored in a refrigerator between 2°C to 8°C until its expiry date. Once removed from the refrigerator, the unopened vial can be stored at room temperature for up to 7 days at a temperature not exceeding 30°C. Vials stored at room temperature can be returned to the refrigerator but the total time the vial can be stored at room temperature must not exceed 7 days. For further advice on the storage of Hemlibra® contact your haemophilia treatment centre.

Hemlibra Ancillaries

To draw up and administer Hemlibra you will be provided with a convenience kit. The contents of the convenience kit may be updated from time to time. Currently, the kit contains vial adaptors or filter needles (x 12 or x 24) syringes (x

12), subcutaneous needle with safety shield (x12) and other supplies as required. You must use one adaptor or filter needle for every vial used. There are currently two different kits available; one which contains a 1ml syringe and another which contains a 2ml syringe. You will be supplied with the kit that best suits your treatment requirement.

The frequency of kit delivery will be determined by the number of adaptors or filter needles used per dose. You must use a separate adaptor or filter needle for every vial you draw up. You should link in with the home delivery company to determine the frequency of kit delivery.

What happens if I switch from my current treatment to Hemlibra®?

When you start on Hemlibra®, you will need to attend your treatment centre to be trained up on how to draw up and administer your Hemlibra®. Your treatment centre will also monitor you for any side effects to Hemlibra®. Once you have been fully trained and feel confident to draw up and administer your Hemlibra dose you can start to self-administer your treatment at home. FVIII prophylaxis may be given for the first 7 days of Hemlibra® treatment, and you will discuss this with your clinician. Your doses will be delivered to your home prior to commencing Hemlibra®. You will be advised by the treatment centre as to which vials you need to bring with you for each dose.

Are there people for whom Hemlibra® may not be suitable?

This will be discussed with you by the doctor at your haemophilia treatment centre. Hemlibra® may not be suitable for:

- People with a past history of thrombosis or significant risk factors for thrombosis
- People with a past history of FVIII inhibitors
- People with severe kidney or liver disease

What happens if I have a bleed?

Hemlibra® prevents bleeds, but it is not a treatment for bleeding. When you switch

to Hemlibra®, check with your haemophilia team how to manage a bleed or injury – it may be different to what you've done in the past or you may need a lower dose because you are having Hemlibra® .

In the first few months after starting Hemlibra®, it is best to contact your treatment centre for advice if you do have a bleed or injury. If your bleed needs further treatment, you treat with FVIII concentrate but only after discussing with your team.

Apart from your haemophilia medication, treat bleeds as you normally would, with PRICE – protection, rest, ice, compression and elevation.

Will I still have to record my Hemlibra treatments on the Homescan app?

Yes, it is important that you keep a record of all your treatment and any bleeds on the home scanning app (mpro5HX) This helps you and your haemophilia team to monitor how well Hemlibra® is working.

Emergency treatment

If an individual with haemophilia presents at an Emergency Department with a bleeding episode which requires treatment, it is important to be seen and treated as quickly as possible. To avoid delays it can be helpful to do the following:

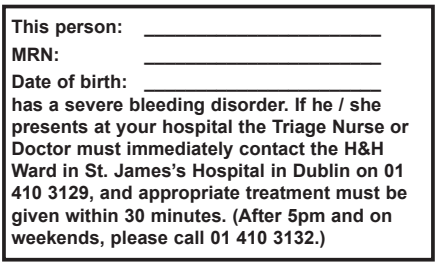
- Show your Bleeding Disorder Registration Card and your Severe Bleeding Disorder Alert Card.

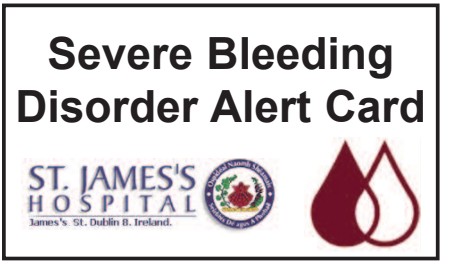
For the person with haemophilia, the most important piece of equipment in a non-specialist centre is the telephone and the instruction to the Emergency Department staff to call the relevant centre.

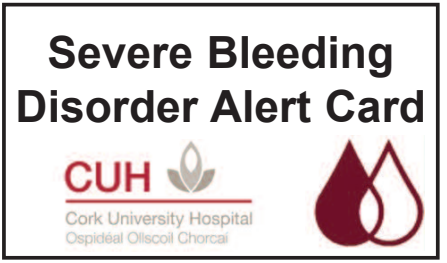
- Show the alert card for Hemlibra®. This will be given to you when you start Hemlibra®.

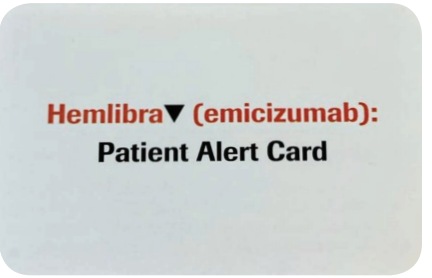
- Call your Comprehensive Care Centre or Haemophilia Treatment centre Or ask a family member to do so. It helps if your Haemophilia team knows that you are in the Emergency Department, no matter which hospital you are in.

Please always remember to carry your Severe Bleeding Disorder Alert Card, Bleeding Disorder Registration Card and Hemlibra card with you at all times.


This person: _____
MRN: _____
Date of birth: _____
has a severe bleeding disorder. If he / she presents at your hospital the Triage Nurse or Doctor must immediately contact the H&H Ward in St. James's Hospital in Dublin on 01 410 3129, and appropriate treatment must be given within 30 minutes. (After 5pm and on weekends, please call 01 410 3132.)







References

Emicizumab (Hemlibra®), Summary of product characteristics-patient insert leaflet, European Medicines Agency (EMA), Accessed 8th February 2020.

Irish Haemophilia Society

Representing people living with haemophilia, von willebrand's and other inherited bleeding disorders

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Twitter: @HaemophiliaIrl

Don't forget you can contact us at the Society on 01 6579900 for further information on any of the above. More information can be found on the Irish Haemophilia Society website; haemophilia.ie

Haemophilia / vWD Treatment Centres in Ireland

Adults

National Coagulation Centre, St. James's Hospital, Dublin 8
Director: Dr. Niamh O Connell
Tel: (01) 416 2141 / 4162142
E-Mail: ncc@stjames.ie

Children

Children's Health Ireland at Crumlin, Dublin 12
Director: Dr. Beatrice Nolan
Haemophilia nurse specialist Tel: (01) 4096939 / 4096940
Tel: (01) 4096100 pager 8731 / 8732 / 8733

After 6pm and at weekends
Tel: (01) 4096100 ask for haematology doctor on call

Non urgent enquiries: haemophilia.dept@olchc.ie
E-Mail : haemophilia.dept@olchc.ie

Adults & Children

Cork University Hospital
Director: Dr. Cleona Duggan
Tel: 021-492 2278 direct line. Hospital line 021-4546400 bleep 719
E-Mail: hcd@hse.ie

After 5pm and at weekends
Tel: 021-4546400 ask for haematology team on call

Galway University Hospital
Director: Dr. Ruth Gilmore
Tel: 021-492 2278 direct line. Hospital line 021-4546400 bleep 719

After 5pm and at weekends
Tel: 021-4546400 ask for haematology team on call

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