

Haemoquest

ADVENTURES IN HAEMOPHILIA A

A guide for people with haemophilia A (congenital factor VIII deficiency) with inhibitors to factor VIII who have been prescribed Hemlibra® (emicizumab)



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HEY!

I'M MICHAEL AND I
HAVE HAEMOPHILIA A
WITH INHIBITORS
TO FACTOR VIII



Your guide to Hemlibra

You have been prescribed Hemlibra to help manage your haemophilia A, because you have inhibitors to factor VIII. Inside this booklet, we'll go on a quest to collect the information you need to know about taking Hemlibra.

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HaemoQuest

Starting a different treatment for haemophilia A can be exciting but it might also be confusing to begin with. HaemoQuest will help you learn a bit about Hemlibra so that you can get the most out of your treatment.

-  Hemlibra is not a cure for your haemophilia A, but if you take it regularly, Hemlibra might reduce the number of bleeds you have
-  This booklet may not answer all the questions you and your caregivers have about Hemlibra
 - In addition to this booklet, before administering Hemlibra you should read the package leaflet contained in the box with your medicine, the guide for patients/carers and the patient alert card your doctor or nurse will have provided
 - You can also talk to you doctor or nurse if there is anything else you would like to find out

Who else can help you to learn about Hemlibra?



DUDE!

I'M CHRIS, MICHAEL'S BEST
FRIEND. WE'RE
GOING ON A QUEST
TO LEARN ABOUT A
MEDICINE CALLED
HEMLIBRA

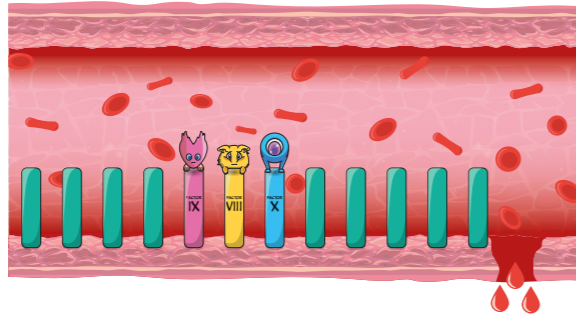


LET'S GO!

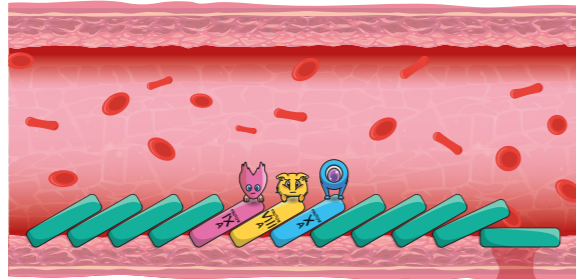
LET'S FIND OUT
MORE ABOUT
HAEMOPHILIA A

What is haemophilia A?

There are things in your blood called **clotting factors** that work together to make a clot. Three of these are **factor IXa** (pronounced activated factor 9), **factor VIII** (pronounced factor 8) and **factor X** (pronounced factor 10)

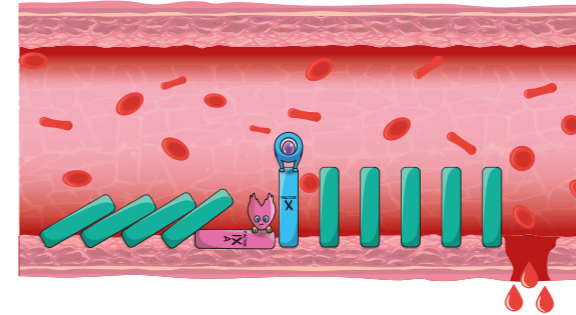


Clotting factors interact with each other in a sequence – think of them like a set of dominoes.



Each clotting factor switches on the next one. When all the clotting factors have been switched on a clot is formed.

If you have haemophilia A, your blood does not clot properly. People with haemophilia A do not have enough of one of these blood clotting factors, called **factor VIII**.



This is a bit like having a domino missing.

People with haemophilia A are often given **factor VIII replacement therapy**.

This medicine can be really helpful for people with haemophilia A, but sometimes it can stop working. This is because factor VIII is not made by your body. Your body can sometimes think that the factor VIII replacement therapy does not belong there. As a result, **inhibitors** can form.



HELLO!

I'M DR PHILLIPA.
THE CLOTTING
PATHWAY IS A BIT LIKE
DOMINOES FALLING.

CAN YOU MAKE A
DOMINO CASCADE?



WATCH OUT!

THE INHIBITORS HAVE STOPPED MY FACTOR VIII REPLACEMENT THERAPY FROM WORKING!

Inhibitors

An inhibitor

Inhibitors are antibodies that stick to factor VIII replacement therapy in your blood



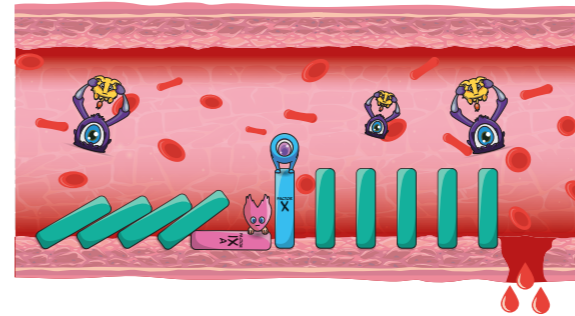
Factor VIII replacement

Your body uses factor VIII replacement therapy to make blood clots and stop bleeds

AN INHIBITOR HAS GRABBED THE FACTOR VIII...

What are inhibitors?

Inhibitors are antibodies that stick to factor VIII in the medicine. When this happens, you have **'haemophilia A with inhibitors to factor VIII'**. Like you and Michael, one in three people with severe haemophilia A start to make inhibitors to factor VIII at some point in their lives



Remember the dominoes?

The inhibitors stick to factor VIII, taking the domino out of the chain. This means the blood cannot clot properly.

HaemoFacts

- Inhibitors are a type of **antibody**
- Antibodies are a normal part of your blood
- They usually help to fight infections



LET'S GO!

WE'RE GOING TO LEARN EVERYTHING WE CAN TO HELP MICHAEL IF HE HAS A BLEED

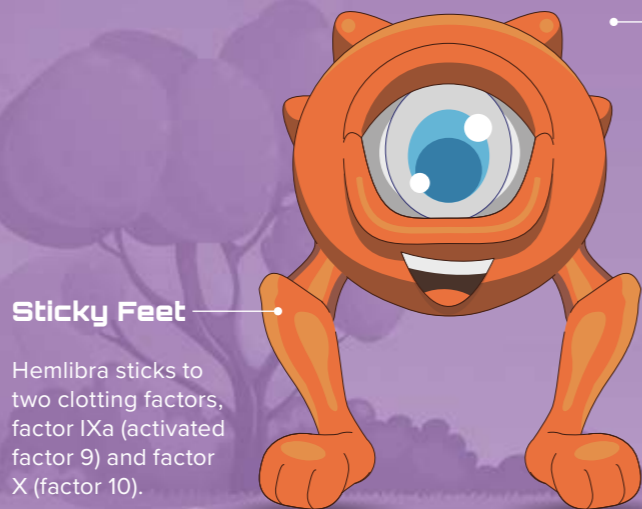


SO HEMLIBRA CAN HELP STOP BLEEDS EVEN IF YOU HAVE INHIBITORS TO FACTOR VIII?

Antibodies

Antibodies are a normal part of your blood that help fight infection. They help to protect you by recognising and sticking to things that shouldn't be in your body, such as bacteria or 'germs'.

Antibodies can also be made in a laboratory and used as medicines.



Sticky Feet

Hemlibra sticks to two clotting factors, factor IXa (activated factor 9) and factor X (factor 10).

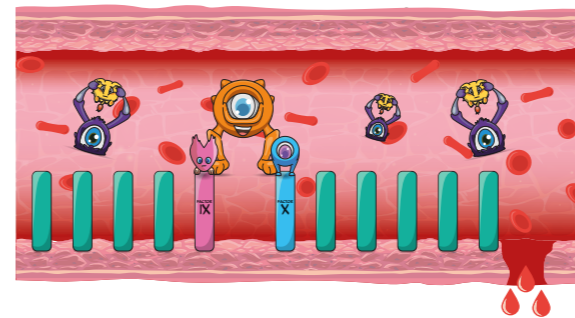
Hemlibra

Dr Phillipa has made an antibody that can help people with haemophilia A with inhibitors to factor VIII.

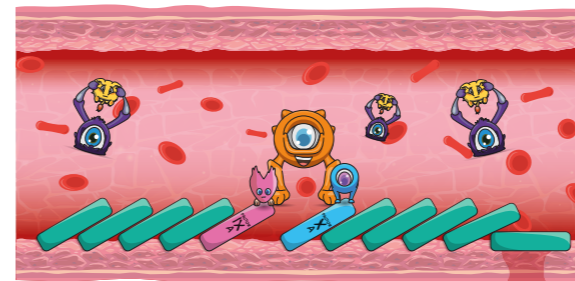
It should still work even if you have inhibitors to factor VIII

HEMLIBRA IS HERE TO HELP...

How does Hemlibra work?



Hemlibra is different, as it doesn't try to replace your missing factor VIII. Instead, Hemlibra creates a bridge between factor IXa and factor X that you do have in your blood.



By creating this bridge Hemlibra allows the rest of the clotting factors to continue working together to form a clot.

Because Hemlibra is not the same as factor VIII replacement therapy, inhibitors to factor VIII shouldn't stick to Hemlibra to stop it from working



GREAT NEWS!

WE DON'T HAVE TO WORRY ABOUT THE FACTOR VIII INHIBITORS GRABBING HOLD OF HEMLIBRA!

HEMLIBRA IS DIFFERENT TO FACTOR VIII REPLACEMENT THERAPY IT IS DESIGNED TO GIVE YOU STABLE LEVELS BETWEEN DOSES

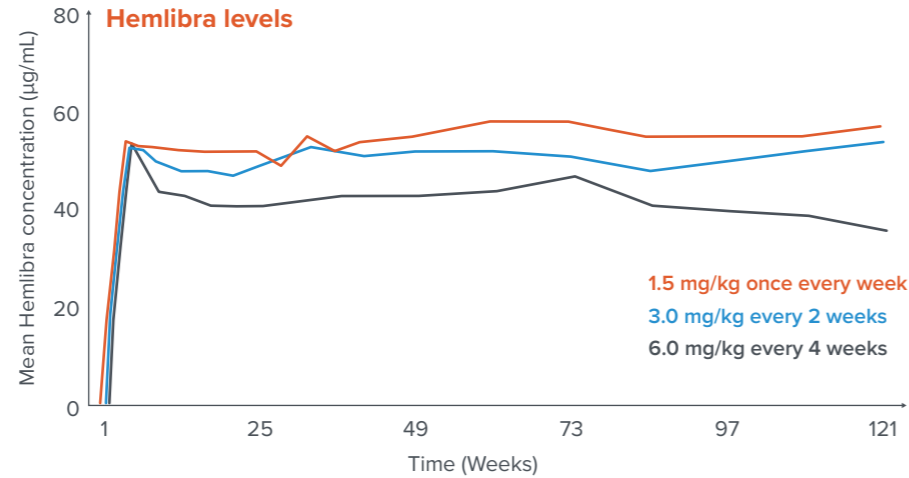


The science part

Hemlibra

After the initial four starting (also called loading) doses of 3.0 mg/kg once a week, you will take Hemlibra once every week, once every 2 weeks, or once every 4 weeks, depending on the schedule you and your doctor or nurse have decided on.

Hemlibra levels remain stable between doses. **This means that you do not need to take additional doses of Hemlibra to cover activities such as playing sport.**

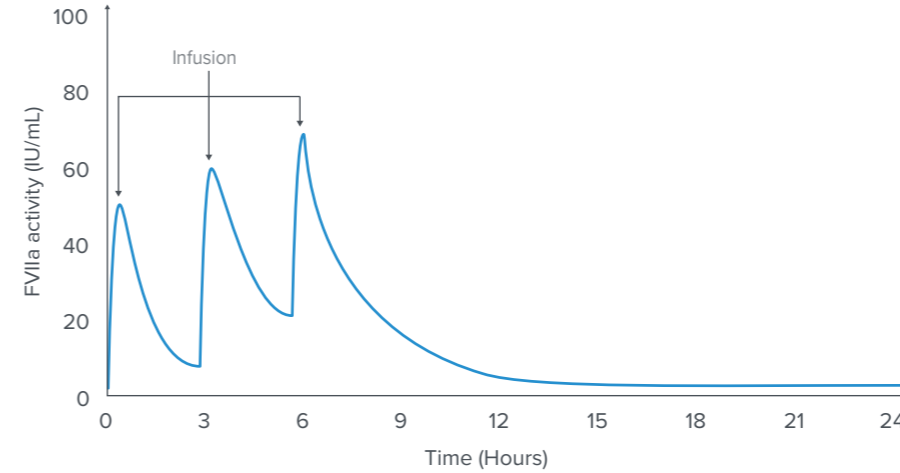


(adapted from Callaghan *et al*, *blood* 2021)

Bypassing agents

The level of bypassing agent therapy falls following administration, meaning repeat doses may be required to manage bleeds.

This example shows the peaks and troughs in recombinant factor VIIa therapy with repeat doses (such as NovoSeven).



(adapted from Stenmo C, Fernandez-Bello I, Ezban M, *et al*. *Blood*. 2014;124:2824)



COOL!

REMEMBER, YOU DON'T TAKE ADDITIONAL HEMLIBRA WHEN YOU WANT TO GO AND PLAY SPORTS




GET INTO A ROUTINE!




DON'T FORGET TO TAKE HEMLIBRA REGULARLY AS INSTRUCTED BY YOUR DOCTOR OR NURSE

Taking Hemlibra

Hemlibra must be taken regularly to help prevent bleeds. This type of treatment is called **prophylaxis**.

-  **Your doctor or nurse will tell you how often to take your Hemlibra. It is important that you try not to forget any injections so that you have a better chance of preventing bleeds**

You can use the dosing card in this pack to help keep track of your injections and remember your dose. You should also record your treatment in the Haemtrack® app

-  **Take Hemlibra regularly, as instructed, even if you have not had a bleed in a while**
-  **Do not take extra Hemlibra if you have a bleed.**
-  **Do not change the dose of Hemlibra unless your doctor or nurse tells you to. For example, do not take extra Hemlibra if you are planning to take part in sport**



CAN YOU HELP HEMLIBRA FIND A WAY THROUGH THE MAZE TO MICHAEL WHEN INHIBITORS HAVE GRABBED FACTOR VIII?



REALLY?

WHEN IT WAS BEING TESTED SOME PEOPLE WHO TOOK HEMLIBRA DIDN'T HAVE ANY BLEEDS

What people say about Hemlibra

Hemlibra has already been tested in people like you and Michael who have haemophilia A with inhibitors to factor VIII.

When Hemlibra was taken regularly, children and adults reported:

- Having less bleeds that needed treatment with bypassing agents. Many people did not have any bleeds that needed treatment with bypassing agents^{1,2}

What is a bypassing agent?

- Bypassing agents are treatments for haemophilia A with inhibitors to factor VIII. They help blood to clot when factor VIII replacement therapy does not work any more
- You may have already taken bypassing agents. These are called:
 - Activated prothrombin complex concentrate (aPCC, Feiba)
 - Recombinant activated factor VII (rFVIIa, NovoSeven)

References: 1. Oldenburg J, et al. *N Engl J Med.* 2017;377:809–818 2. Young G, et al. *Blood.* 2019;134(24): 2127-2138.

ARCHERY KGB JTNL JBF EGB IMLP
 IMNGVBKNBVFNGBADMINTONUM
 PJBFBMLMHFVNMLMHGFVHPLN
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 IKLHKUIKHFROHLRJLGOLF TCO
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 TDTHDIYUOTFGRDOIPNTCRESU
 ILJYRCSFHKOPSWIMMINGORS
 NAHKOTVEOGIMALPHEVUHEBJR
 GIUTRPUTSMTABLETENNISTCA
 RFINOQSGHTBINTSIMONTLEDW
 OPVEWLEDORVEDOTHQAOTVINI
 VESTIUTBEDWALKINGLINTDEN
 XIGENLECIEBT SINTECINENFG
 OTVPGQUBITNEDSINTHINEDWD
 QIBTLIREADINGKOEDINTNEVJ
 TKEDVIPRCEGQLICYCLINGLAI

Answers: archery, badminton, golf, swimming, walking, rowing, cycling, table tennis, drawing, painting, reading, video games



WORD UP!

MICHAEL DOES 12 DIFFERENT ACTIVITIES EVERY MONTH! CAN YOU FIND THEM ALL?



Getting into a routine with Hemlibra

Using your weight, your doctor or nurse will work out how much Hemlibra you should take.

- **For the first 4 weeks, you take a starting (or loading) dose once a week (3.0 mg/kg)**
- **After that, you carry on taking your normal maintenance dose.** This will be either: (tick your dose schedule)

once every week
(1.5 mg/kg)

once every 2 weeks
(3.0 mg/kg)

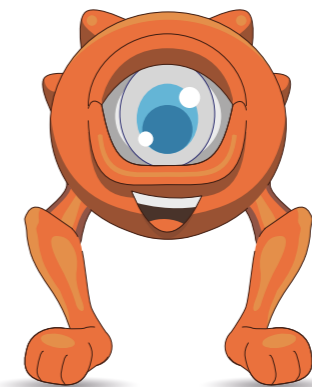
once every 4 weeks
(6.0 mg/kg)

What day do you plan to take your Hemlibra?

Your doctor or nurse will decide how often you should be weighed. This is a time when you are growing fast, so they need to make sure you are taking enough Hemlibra. Even if your weight does increase, do not change your dose of Hemlibra without talking to your doctor or nurse.

You must stop taking bypassing agents the day before you start taking Hemlibra. Before you start taking Hemlibra, you and your caregiver should read the package leaflet contained in the box with your medicine, the guide for patients/carers and the patient alert card.

If you need to have any laboratory or blood tests, tell the healthcare team that you are taking Hemlibra. Taking this medication can interfere with some of these tests, giving incorrect results.



GREAT!

I ALWAYS TAKE MY
HEMLIBRA ON THE SAME
DAY OF THE WEEK AND AT
THE SAME TIME OF DAY
SO IT'S EASY
TO REMEMBER!



HEY!

CAN YOU HELP ME
FIND THE INHIBITORS?

THERE ARE FOUR HIDDEN
AMONG SOME
CLOTING FACTORS
OVER THERE...



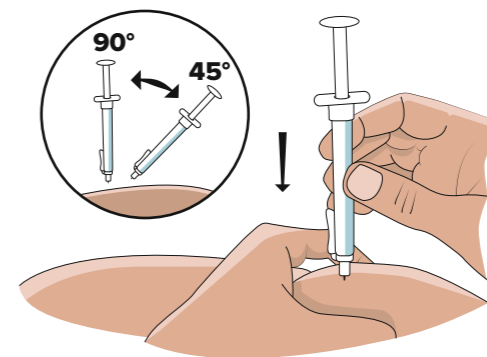
Hemlibra injections

↓ Hemlibra is given by an injection under the skin.
This is called a **subcutaneous injection**

👤 This is a different way
to give treatment for
haemophilia A. Your
doctor or nurse will help
you and your caregiver
to learn how to give
subcutaneous injections

📌 Hemlibra injections
should be given at an
angle of between
45°-90° to the skin

📺 There is a video that might also help.
Scan the QR code to the right,
or visit www.takingemicizumab.com





REMEMBER!

WASH YOUR HANDS,
CLEAN YOUR SKIN AND
CHANGE THE AREA
OF YOUR INJECTION
EACH TIME

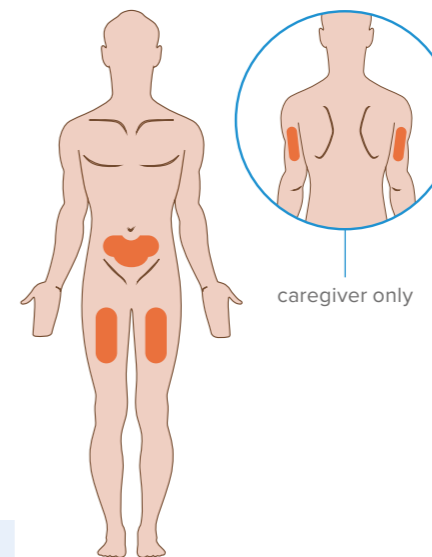
Preparing for Hemlibra injections

- * Make sure you (or the person giving the injection) wash your hands well with soap and water before preparing and injecting Hemlibra
- ✓ The administration mat with this pack lists everything you need for your injection
- 🕒 Before use, allow the vial(s) to reach room temperature for about 15 minutes on a clean flat surface away from direct sunlight
- ↔ For each injection, use a different area of the body to the one you used last time. Each injection should be at least 2.5 cm away from the area you used for your last injection. This also applies if your dose is given with more than one Hemlibra injection
- ☀ Unless your doctor or nurse has told you not to, clean the chosen area using an alcohol wipe and let the skin dry for about 10 seconds
- ! Do not inject into areas that could be irritated by a belt or waistband. Do not inject into moles, scars, bruises, or areas where the skin is tender, red, hard or if the skin is broken

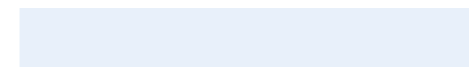
Where to inject Hemlibra

Hemlibra injections should only be given into certain parts of your body:

- Your thigh (front and middle)
- Your stomach area, except for 5 cm around the belly button
- The outer area of your upper arm (only if someone else is giving the injection)



Who can help with giving your injections?



- 📍 You can find more information about injecting Hemlibra on page 26, in the instructions in the Hemlibra package leaflet contained in the box with your medicine and the guide for patients/carers



LOOK!

THIS PICTURE SHOWS
THE AREAS OF THE
BODY THAT I SHOULD
HAVE MY HEMLIBRA
INJECTIONS

What side effects might I get with Hemlibra?

Like all medicines, Hemlibra can cause side effects, although not everybody gets them.

Very common: may affect more than 1 in 10 people

- A reaction in the area where the injection is given (redness, itching, pain)
- Headache
- Joint pain

Uncommon: may affect up to 1 in 100 people

- 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)
- Destruction of red blood cells (thrombotic microangiopathy)
- Lack of effect or decreased response to treatment
- Swollen face, tongue and/or throat and/or difficulty in swallowing, or hives, together with difficulty in breathing which are suggestive of angioedema

Common: may affect up to 1 in 10 people

- Fever
- Muscle aches
- Diarrhoea
- Itchy rash or hives (urticaria)
- Skin rash

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in the package leaflet. You can also report side effects directly via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard. You should also report side effects to Roche Products Ltd by emailing the Roche Drug Safety Centre at welwyn.uk_dsc@roche.com or calling +44 (0) 1707 367554. By reporting side effects you can help provide more information on the safety of this medicine.

Using bypassing agents with Hemlibra

Before starting Hemlibra, talk to your doctor and carefully follow their instruction on when to use a bypassing agent and the dose and schedule you should use. During the studies of Hemlibra, serious side effects were reported when using aPCC while receiving Hemlibra. Stop using Hemlibra and aPCC and talk to a doctor immediately if you or your caregiver notices any of the following side effects:

Destruction of red blood cells (thrombotic microangiopathy):

- Confusion, weakness, swelling of arms and legs, yellowing of skin and eyes, vague belly (abdominal) or back pain, feeling sick (nausea), being sick (vomiting) or urinating less – these symptoms may be signs of thrombotic microangiopathy

Blood clots (thromboembolism):






- Swelling, warmth, pain or redness – these symptoms may be signs of a blood clot in a vein near the surface of the skin
- Headache, numbness in your face, eye pain or swelling or problems with your vision – these symptoms may be signs of a blood clot in a vein behind your eye
- Blackening of the skin – this symptom may be a sign of severe damage to the skin tissue

If you need to go to hospital for a bleed, make sure you tell the healthcare team that you are taking Hemlibra. Remember to take your patient alert card with you. Refer to your emergency plan on page 25 and read the package leaflet contained in the box with your medicine, the guide for patients/carers and patient alert card for more information.



What happens if I have a bleed?

If you do have a bleed, DO NOT take extra Hemlibra!

-  It is very important you and your caregiver talk to your doctor about what to do in an emergency when you are taking Hemlibra
 -  You might need to take bypassing agents if you have a bleed. If you have used these before, this time it may be different from how you used them in the past
 -  More information on using bypassing agents with Hemlibra can be found on page 23 of this booklet, the package leaflet contained in the box with your medicine, the guide for patients/carers and patient alert card
-  If you need to see a doctor or nurse, make sure that you take your alert card with you
-  If you are using HealthID or have a MedicAlert bracelet or necklace, you could update your information

In an emergency:

Ask your doctor or nurse to write down what to do if you have a bleed.
(Remember to keep this updated, if anything changes).

Signed: _____

Emergency contacts:

Some additional questions you may have

Injecting Hemlibra

Who should I tell if I am having trouble with my injections?

Once you or your caregiver has been trained, you should be able to inject Hemlibra at home, by yourself or with their help. Tell your doctor or nurse if you are not confident with performing subcutaneous injections.

What if the Hemlibra vial or liquid looks strange?

Inspect each vial before use. Do not use if they appear damaged, the cap covering the stopper is missing or if they have been dropped. Before using Hemlibra, check the solution for particles or discolouration. The solution should be colourless to slightly yellow. Do not use if it is cloudy, hazy, discoloured or contains visible particles. Contact your haemophilia centre and provide the batch details of the affected vial. Keep the vial in the correct storage conditions as you may need to return it to your centre.

I'm having trouble getting Hemlibra into the syringe

Hemlibra is quite a thick liquid. If you are performing your own injections, you might find it difficult to get it into the syringe at first. Talk to your doctor, nurse or caregiver and they can help you until you are more confident in taking Hemlibra on your own.

Once I have transferred Hemlibra into a syringe, can I take it later?

No. Once the syringe has been filled with Hemlibra, the injection must be given immediately. Do not refrigerate the syringe with Hemlibra in it.

How should I throw away my needles and syringes?

Any used vials, needles, vial/injection needle caps and used syringes should be placed in a sharps bin or puncture-proof container. Make sure that you use new needles and syringes for each injection and dispose of them after a single use.

If I do not use all the Hemlibra in a vial can I save it for the next injection?

No. Only use the vial once. After you inject your dose, throw away any unused Hemlibra left in the vial.

Where I inject my Hemlibra is sore afterwards, what should I do?

This is a very common side effect that some people get with Hemlibra. Make sure that you change the area that you are using after each injection. If you have signs of redness, itching or soreness tell your doctor or nurse.

Some additional questions you may have

Taking Hemlibra

Should I tell people I have started taking Hemlibra and changed medications?

Your regular haemophilia A team, including your nurse and GP, will be told when you change medications. If you are using HealthID or have a MedicAlert bracelet or necklace, remember to update your details. It is up to you whether you tell your friends, family or a teacher about your treatment, but it may help to talk to people that are close to you so that they can support you.

How long will I be on Hemlibra for?

Hemlibra is intended for long-term treatment. Usually you will continue taking Hemlibra as long as you and your doctor or nurse are happy with how your treatment is going. Some people have taken Hemlibra for over five years.

Can I take more Hemlibra if I wake up with pain?

No, If you think that you are having a bleed, do not take extra Hemlibra. Your caregiver might take you to see your doctor or nurse about your pain.

If I have not had a bleed in a while, can I stop Hemlibra?

Even though it is good news that you have not had a bleed in a while, you still need to keep taking Hemlibra so you have a better chance of continuing to prevent bleeds in the future. Do not stop taking Hemlibra without talking to your doctor or nurse.

Can I have a break from taking Hemlibra?

Make sure you do not stop taking Hemlibra without talking to your doctor or nurse.

Are there any medications that I should not take with Hemlibra or need to be careful with?

Stop taking any treatment with bypassing agents (aPCC, Feiba and rFVIIa, NovoSeven) the day before starting Hemlibra.

Because Hemlibra helps your blood to clot, taking other clotting medicines at the same time can make the blood clot too much! You or your caregiver should only use aPCC if advised to do so by your haemophilia A care team. Also read page 23 of this booklet, the package leaflet contained in the box with your medicine, the guide for patients/carers and patient alert card for more information.

I forgot to take my Hemlibra, what do I do?

If you forget your scheduled injection, inject the forgotten dose as soon as possible up to the day before the day of the next scheduled dose. Then, inject Hemlibra as scheduled. Do not inject two doses on the same day to make up for a forgotten dose. If you are not sure what to do, ask your doctor or nurse.

Should I take more Hemlibra if I am going to play sport?

No. You must only take Hemlibra as prophylaxis regularly, as instructed. When Hemlibra was tested, people had stable levels of Hemlibra in their blood for the whole time between injections.

Some additional questions you may have

Storing Hemlibra

How do I store Hemlibra at home?

Hemlibra needs to stay pretty cool – store your Hemlibra vials in your fridge (2°C to 8°C) in the original box. Do not freeze Hemlibra and do not shake the vials. Remember to check the expiry date written on the side of the box and on the vial label (the date refers to the last day of the month).

Can I take Hemlibra out of the fridge?

Once removed from the fridge, unopened vials can be kept at room temperature (below 30°C) for a total of 7 days. Discard any vial that has been kept at room temperature for more than 7 days or that has been in temperatures above 30°C.

Lifestyle

What activities are OK to do?

When you have haemophilia A, it's really helpful to stay active when you can. When taking Hemlibra, you can carry on with the hobbies and sports that you usually enjoy; from reading and painting to going cycling or swimming with friends.¹ Talk to your doctor or nurse first if you want to try any new activities.

Do I need to change what I eat?

You do not need to change your diet when you are taking Hemlibra, but it is important for anyone with haemophilia A to try to be as healthy as possible; eat well and make sure you drink plenty of water. You can find lots of information about staying healthy with haemophilia A from places like The Haemophilia Society or the World Federation of Hemophilia.

Reference: 1. Srivastava A, et al. *Haemophilia*. 2013;19:e1–47

Any other questions?

If you have any other questions about Hemlibra, write them down here so you remember to ask your doctor or nurse the next time you have an appointment.

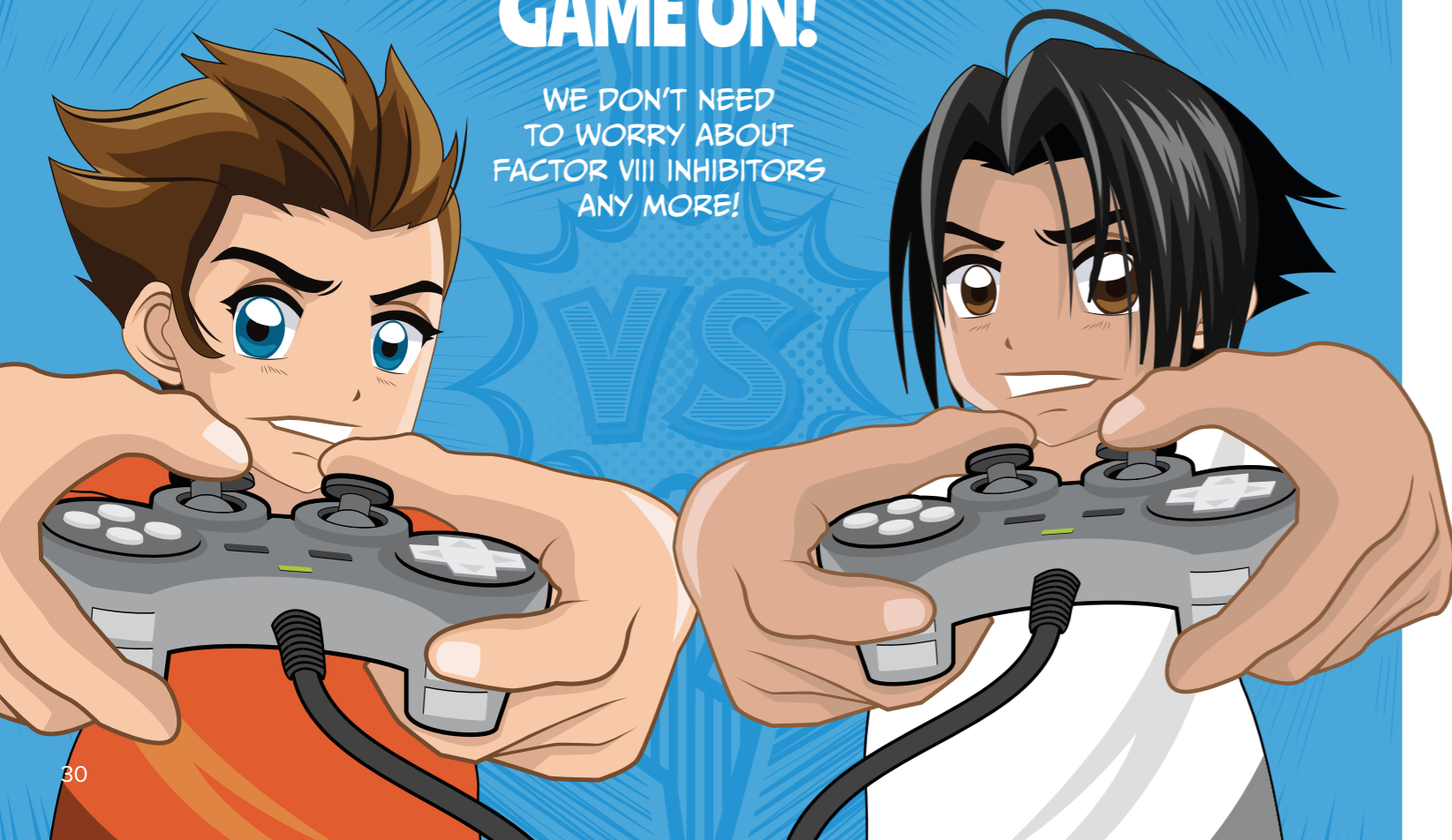


REMEMBER!

IF YOU NEED
TREATMENT FOR
A BLEED, TELL THE
DOCTORS OR NURSES
THAT YOU ARE
TAKING HEMLIBRA

GAME ON!

WE DON'T NEED
TO WORRY ABOUT
FACTOR VIII INHIBITORS
ANY MORE!



Glossary

Here is a list of some words that we talked about in this booklet and their meanings

Antibody

Tiny things made by your blood that help to fight infection by sticking to substances in your blood that should not be there

Clotting

To stop a bleed, blood changes from a liquid into a gel in the area that is damaged, for example, a small cut in a vein. The clot blocks the hole to stop blood from leaking out

Clotting factors

In your blood you have many things called clotting factors that work together to help make your blood clot

Factor VIII

The clotting factor that you are missing or have low amounts of in your blood when you have haemophilia A

Factor VIII replacement therapy

A medicine that replaces the low or missing factor VIII in the blood of people with haemophilia A

Haemophilia A

A bleeding disorder where people are missing or have very little factor VIII. Haemophilia A can be described as mild, moderate or severe depending on how much factor VIII is in the blood

Inhibitor

A type of antibody that can stop factor VIII replacement therapy from working

Prophylaxis

The regular use of a treatment to prevent illness. For people with haemophilia A, prophylaxis is intended to prevent bleeding from occurring or reduce the number of bleeds that you have

Subcutaneous injection

A way to give medicine that involves injecting a small amount just beneath the skin

SPECIAL THANKS GOTO...

JULIA SPIRES,
CLINICAL NURSE SPECIALIST,
HAEMOPHILIA COMPREHENSIVE
CARE CENTRE,
GREAT ORMOND STREET
HOSPITAL

SIMON FLETCHER,
LEAD RESEARCH NURSE,
OXFORD HAEMOPHILIA
AND THROMBOSIS
CENTRE, CHURCHILL HOSPITAL

**FOR THEIR HELP AND
GUIDANCE DURING THE
DEVELOPMENT OF THESE
MATERIALS**

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in the package leaflet. You can also report side effects directly via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard. You should also report side effects to Roche Products Ltd by emailing the Roche Drug Safety Centre at welwyn.uk_dsc@roche.com or calling +44 (0) 1707 367554. By reporting side effects you can help provide more information on the safety of this medicine.