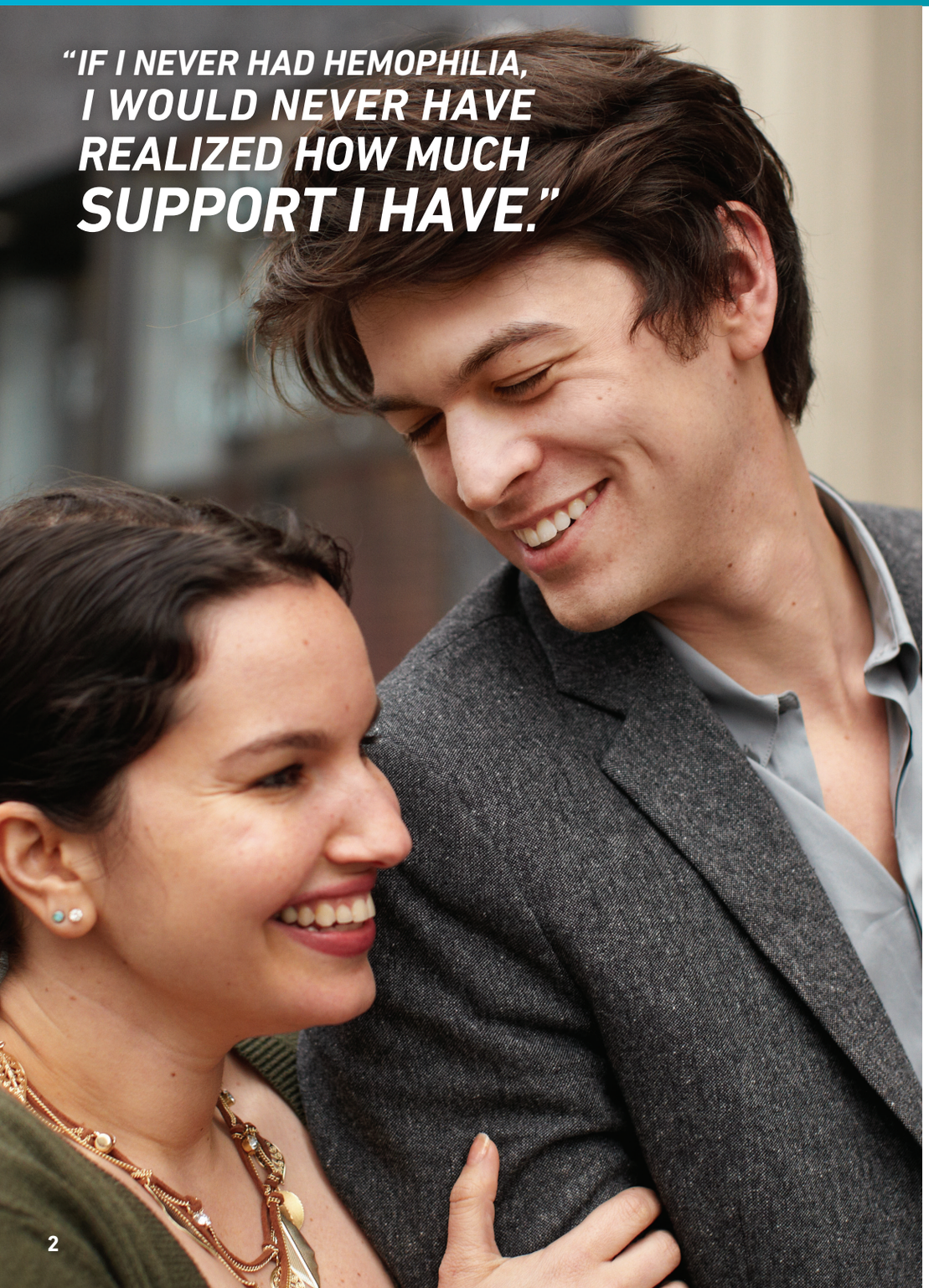
GETTING TO KNOW BENEFIX

An information booklet for patients

Pr BeneFix® Coagulation Factor IX (Recombinant)

Pfizer



GETTING TO KNOW BENEFIX

Pfizer wants you to know as much as possible about your condition and its treatment. The purpose of this booklet is to provide information to patients and persons interested in the treatment of hemophilia B. It is important to remember that the booklet is a guide and not a replacement for discussion regarding your disorder with the hemophilia nurses and doctors of your team.

What is hemophilia B?

People with hemophilia B (sometimes called "Christmas disease") either do not have enough FIX ("factor nine") in the blood, or have no FIX protein for clotting to take place if they become injured. When an injury occurs, and a blood vessel is damaged the person may lose a significant amount of blood, or bleed into their soft tissue, muscles or joints, damaging them.

What is BeneFIX?

BeneFIX is a coagulation factor, created using recombinant DNA technology. It is used to replace clotting FIX and to stop or prevent bleeding in people with hemophilia B who do not have enough FIX of their own.

Does BeneFIX work for other coagulation factor deficiencies?

No – BeneFIX is the recombinant product used to treat patients with a FIX disorder and should not be used for other bleeding problems, for example bleeds caused by:

- Shortages of other clotting factors (II, VII, and X)
- Low levels of liver-dependent coagulation factors
- Coumarin-induced anticoagulation

How is BeneFIX made?

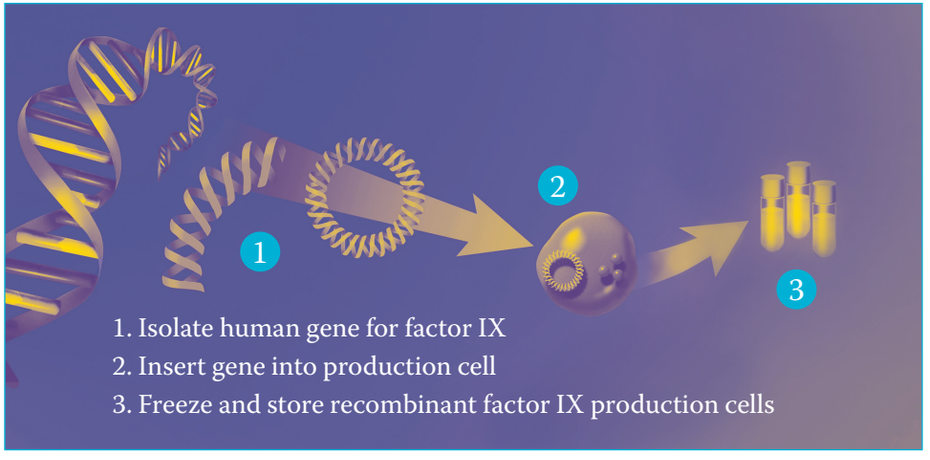
BeneFIX is manufactured using recombinant DNA technology, which lets the makers of BeneFIX produce it without using human blood or plasma products, keeping it free of viruses or bacteria that might cause infection. Many commonly used drugs have been created by recombinant technology.

Recombinant DNA refers to pieces of DNA that have been isolated from one type of cell, and "recombined" or inserted into the DNA of a different type of cell (recombinant cell). The recombinant cells are then placed in specially made containers, called bioreactors. There the cells grow, multiply and produce large amounts of the protein coded by the recombinant DNA.

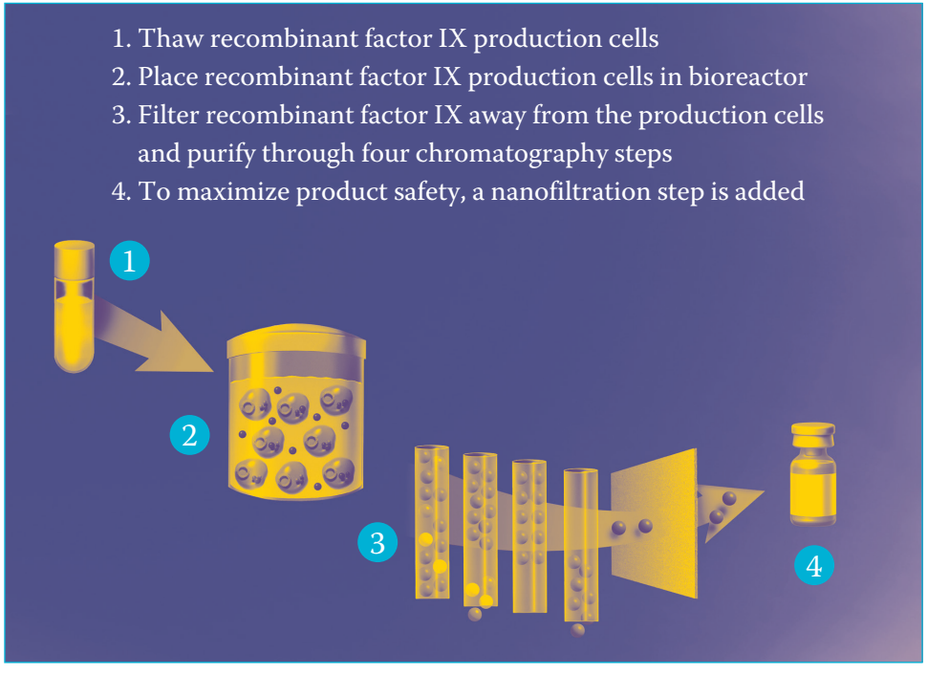
In the case of BeneFIX, the cells make recombinant FIX. The cells used to make BeneFIX are derived from Chinese hamster ovary cells, a cell line that has been extensively studied and shown to be free of infectious agents.

Even though BeneFIX is manufactured using recombinant technology, four chromatography steps and a nanofiltration step are included to purify the BeneFIX and further reduce any potential risk of viral exposure. After purification, the recombinant FIX is formulated and freeze-dried as BeneFIX.

Stage 1: Creating Recombinant Factor IX Production Cells



Stage 2: Producing BeneFIX



What steps are taken to promote the viral safety of BeneFIX?

Pfizer uses a multi-step approach to promote viral safety for BeneFIX:

- BeneFIX is not derived from human plasma.
- The manufacturing process and formulation do not use added human or animal protein.
- The Chinese hamster ovary cell line used to grow the production cells for BeneFIX has been extensively studied and used.
- The cells used to make BeneFIX are routinely tested.
- The cells growing in the bioreactor are routinely monitored.
- The multi-step purification process has been designed to eliminate most known viruses.

I'm scheduled for surgery next month, are there any issues I should be aware of?

With the help of coagulation factor products, patients can be treated during both major and minor surgical procedures. Your healthcare team will monitor your progress to ensure your FIX levels are correct. BeneFIX has been used during many types of surgery, including liver transplantation, orthopedic procedures and dental surgery. After surgery it is important to have adequate factor in your blood to prevent bleeding. You should follow the specific instructions provided by your healthcare team.

Always contact your hemophilia treatment centre prior to any minor or major surgery, including dental procedures, or any invasive procedure.

What is recovery?

The recovery level of FIX tells healthcare providers how much your circulating FIX levels in your blood stream have increased after your infusion. Recovery can vary from patient to patient and can be influenced by age and weight. Your hemophilia doctor or nurse may check your recovery level of FIX and adjust your dose to ensure the appropriate response is reached for bleeding episodes and procedures.

What about inhibitors?

An inhibitor is an antibody that develops towards your factor and reduces the clotting action of the factor product. The incidence of inhibitor production in hemophilia B patients is less common than in hemophilia A. In most cases, these inhibitors develop after the first infusions of FIX and can sometimes be accompanied by allergic reactions.

The initial 10 to 20 infusions should therefore be performed under appropriate medical supervision where proper medical care for allergic reactions can be provided. The risk of inhibitor development with BeneFIX is generally very low.

Tell your doctor immediately if you are using increased amounts of BeneFIX in order to control a bleed as this might be caused by an inhibitor. As with all factor IX products, patients using BeneFIX should be monitored for the development of factor IX inhibitors.

Are there any side effects I should know about?

The initial doses of BeneFIX are administered in the hemophilia treatment centre, where your response and any side effects you may experience can be monitored by your healthcare team. Some of the side effects include headache, runny or stuffed nose, light headedness, fever, chills, flushing, nausea, vomiting, diarrhea, lethargy, discomfort or swelling at the injection site, altered taste, cough, burning sensation in the jaw or skull and changes in your vision.

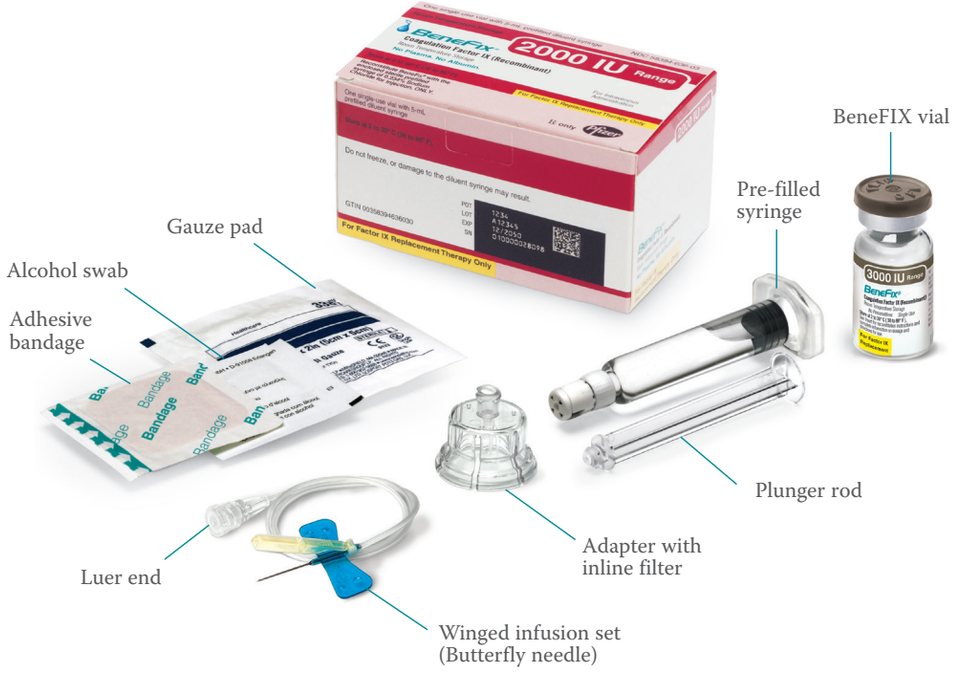
If you experience these mild side effects from injecting BeneFIX later at home, they should usually disappear on their own. If they continue or if you are concerned, tell your hemophilia doctor or nurse.

Allergic reactions can occur with all FIX products, including BeneFIX. They are rare, but if you suspect you are having an allergic reaction IMMEDIATELY report it to your hemophilia nurse or doctor.

Allergic reactions can include: rash, itching, chest tightness, laryngospasm, bronchospasm, wheezing, dizziness, hives, faintness, rapid heartbeat, shortness of breath, blurred vision and a swollen face. You should stop using the product and contact your hemophilia centre immediately and/or seek emergency care.

PREPARATION STEPS FOR BENEFIX

The following steps are provided as general guidelines for preparing and administrating BeneFIX. Always follow the specific preparation and administration procedures provided by your hemophilia treatment centre.



- If refrigerated, allow BeneFIX and the pre-filled diluent syringe to come to room temperature.

Aseptic technique (meaning clean and germ free) should always be used when preparing and injecting BeneFIX.

2

- Wash your hands with good soapy lather for a minimum of 30 seconds.

3

- Remove plastic flip top cap.
- Wipe top of vial with alcohol swab.

4

- Remove cover from plastic vial adapter package.
- Place adapter over BeneFIX vial, press down firmly until it snaps into place.
- Leave plastic cover on adapter until you are ready to connect the syringe.

5

- Remove plastic cover on adapter.

6

- Attach plunger rod to diluent syringe by inserting the rod into the syringe and turning.

7

- Remove plastic cap from diluent syringe by bending up and down to break the seal.

8

- Connect the syringe to adapter on BeneFIX vial.
- Insert tip of syringe into adapter opening.
- Push firmly and turn in a clockwise direction.

9

- Slowly push down plunger of syringe to inject all diluent into BeneFIX vial.

- Don't remove syringe.
- Gently swirl vial and invert vial and swirl until all the BeneFIX powder is dissolved.
- Solution should be clear and colourless.

- Invert vial, slowly draw reconstituted BeneFIX into syringe.
- Remove syringe from vial by pulling and turning counter clock-wise.

If using more than one vial

- Prepare all the vials of BeneFIX you need, leaving the diluent syringes attached until you are ready to draw back the solution.
- Remove all of the diluent syringes from the vial adapters, leaving the vial adapters in place.

- Remove the large luer lock syringe from the packaging and attach it to the vial adapter and draw back the BeneFIX solution as in step 11.
- Transfer the large luer lock syringe to the next vial adapter to draw back this BeneFIX solution.
- Repeat these steps with as many vials as required.

Administration (intravenous injection) of BeneFIX

BeneFIX should be administered within 3 hours after reconstitution. The reconstituted solution may be stored at room temperature prior to administration.

1. Inspect the solution. The solution should appear clear and colourless. If you see any specks, or discolouration, discard the solution and start over.
2. Attach the syringe to the luer end of the infusion set tubing provided. Apply a tourniquet and prepare the injection site by wiping the skin well with an alcohol swab provided in the kit.
3. Perform venipuncture. Insert the needle on the infusion set tubing into the vein, and remove the tourniquet. The reconstituted BeneFIX product should be injected intravenously over several minutes. The rate of administration should be determined by the patient's comfort level. Reconstituted BeneFIX should not be administered in the same tubing or container with other medicinal products.
4. Following completion of BeneFIX treatment, remove the infusion set and discard it. Dispose of all unused solution, empty vial(s) and used needles and syringes in an appropriate container for throwing away waste that might hurt others if not handled properly.

Talk to your hemophilia treatment centre if you have any questions about BeneFIX.

Note: Agglutination of red blood cells in the tubing/syringe has been reported with the administration of BeneFIX. No adverse events have been reported in association with this observation. To minimize the possibility of agglutination, it is important to limit the amount of blood entering the tubing. Blood should not enter the syringe. If you can see blood clumping in the tubing or syringe, discard all material (tubing, syringe, and BeneFIX solution) and continue administration with a new package.

How is the dose of BeneFIX determined?

The dose of all FIX products depends on the degree of FIX deficiency, the location and extent of bleeding, the age and weight of the person with hemophilia B, and their general physical condition. Your doctor will decide what the correct dose is.

Generally, however, the dose prescribed will be based on one of the following formulas, depending on the age of the patient:

Adult Patients (≥15 years)

Number of factor IX IU required (IU) = **Body weight** (kg) X **Desired factor IX increase** (% or IU/dL) X **1.2** (IU/kg per IU/dL)

Pediatric Patients (<15 years)

Number of factor IX IU required (IU) = **Body weight** (kg) X **Desired factor IX increase** (% or IU/dL) X **1.4** (IU/kg per IU/dL)

How long can I keep BeneFIX in powder form? After reconstitution?

Prior to the expiration date, BeneFIX may be stored at room temperature (not to exceed 30˚C) or under refrigeration. Store the diluent syringe at 2˚C to 30˚C. Freezing should be avoided to prevent damage to the diluent syringe. Do not use BeneFIX after the expiration date on the label. BeneFIX does not contain a preservative and should be used within three hours after reconstitution.

How is BeneFIX supplied?

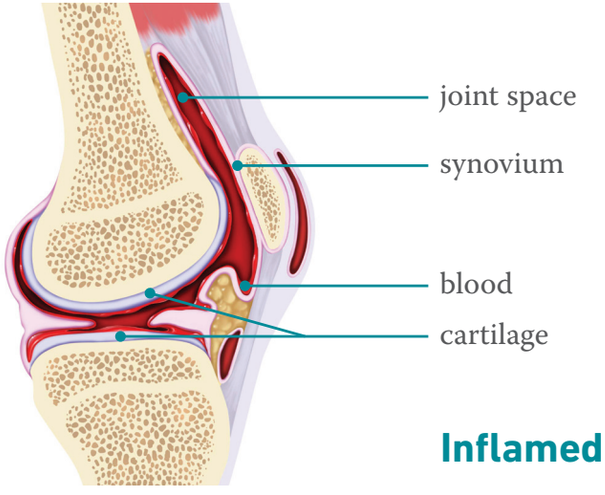
BeneFIX is available in 500 IU, 1000 IU, 2000 IU, and 3000 IU vials. Each kit contains a single-use vial of BeneFIX, one pre-filled diluent syringe, one sterile vial adapter (with inline filter) reconstitution device, one sterile infusion set, two alcohol swabs, one plaster pad and one gauze pad. The actual amount of FIX activity is stated on the label of each vial in international units (IU).

WHAT ELSE CAN I DO TO HELP MANAGE BLEEDS?

1. Be aware of bleeds.

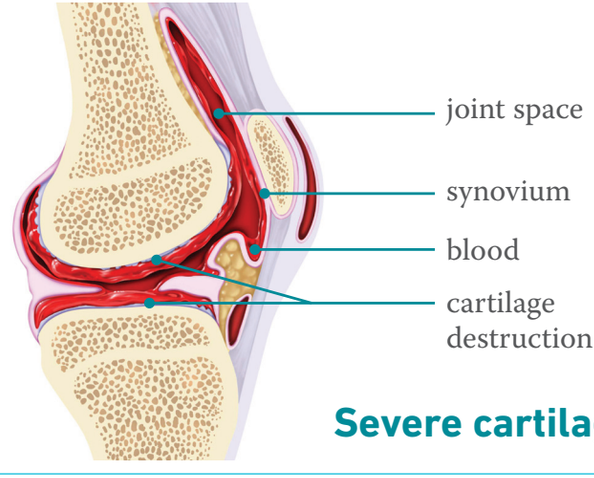
Recognize the early signs of a bleeding problem, such as swelling, pain and bruising. You may be experiencing internal bleeding into your joints or muscles, which can damage these tissues if not treated properly. Seek help from your hemophilia nurse and doctor for immediate treatment. It is just as important to watch for internal bleeds as it is for ones you can see. Treating suspected bleeds immediately can minimize and/or even avoid further joint damage.

As a bleed begins, the space around the knee joint fills with blood.



Inflamed synovium

After many bleeds, the cartilage completely erodes, causing intense pain while hindering movement.



Severe cartilage damage

2. Prevent bleeds

Bleeds can sometimes happen spontaneously. But there are steps you can take to avoid injury and prevent bleeds from happening:

- Taking precautions when participating in activities that could result in injury is always recommended. Choose activities that do not place you at risk for a bleeding problem. Ensure that you wear protective gear such as a helmet every time you engage in potentially high-impact activities. Proper warm-up and stretches before such activities is also recommended.
- Muscle strengthening. Stronger muscles may help protect and support joints. Ask your doctor or physiotherapist if a muscle strengthening program is right for you.
- Preventative clotting factor therapy. Your healthcare provider may recommend taking a regular dose of clotting factor therapy to prevent bleeds before they start, or if you are involved in high activity level sports.

Even with appropriate precautions, some bleeds may still occur. This is when early and complete treatment of each bleed comes into play.

3. Treat each bleed quickly and completely

If you experience a bleed, if necessary administer a sufficient dose of clotting factor, follow the R.I.C.E. technique immediately and notify your hemophilia treatment centre for treatment.

Rest: use the joint as little as possible.

Ice: *put ice* on the injured area for ten to fifteen minutes, every one to two hours, to control swelling and reduce pain. Remember not to apply the ice directly to the skin, cover the ice pack with a cloth or towel to avoid frostbite.

Compression: *apply pressure* to the joint or muscle bleed by using an elastic bandage to help slow down the bleeding. A tensor bandage will also help keep the joint stable, but remember to remove the tensor prior to going to bed.

Elevation: Remember to *elevate the limb* (above your heart) to avoid blood tracking down to your hands or feet. This will help slow down the bleeding and reduce swelling and pain.

Once you've applied treatment to control the bleed, call your Hemophilia Treatment Centre for advice on what to do next.

REMEMBER: WHEN IN DOUBT, TREAT.

4. Maintain a healthy lifestyle, including healthy weight

This is important for everyone, but for people with hemophilia, there are even more reasons to maintain a healthy lifestyle.

Remember healthy eating and exercise will help to maintain a healthy weight. Patients who are overweight put extra stress on their joints, which can make them vulnerable to damage. Also, changes in weight can have a significant impact on the amount of factor product required to stop a bleeding episode. It is important to watch your weight and let your doctor know if anything changes. He or she may need to change your treatment regime and adjust the dose of BeneFIX to ensure your bleeds are controlled effectively.

To help maintain your weight and overall health, talk to your doctor about ways to incorporate physical activity and healthy eating into your lifestyle.

PROGRAMS AND SERVICES

Further Information
You can obtain further information about our services by calling Pfizer at 1-800-463-6001.

Patient Notification System
The Patient Notification System is a free system that operates 24 hours a day, providing up-to-date product withdrawal or recall information of plasma-derived and recombinant therapies to patients and health care providers. To register with the program, log on to www.patientnotificationsystem.org or call 1-888-UPDATE-U.

Care Until Cure
The Canadian Hemophilia Society, through a grant from Pfizer, has established this research program to support innovative clinical research, including outcomes evaluation, to improve the quality of life of persons with hemophilia and other bleeding disorders. Pfizer has invested over two million dollars in the Care Until Cure Program as part of its long-term commitment to research and support of the hemophilia community.

Twinning Program
Designed to improve hemophilia care in developing countries. This unique partnership with the World Federation of Hemophilia gives people with hemophilia a powerful voice in promoting access to, and improving quality of care worldwide.

National Sponsorship of the Canadian Hemophilia Society
Pfizer supports the Canadian Hemophilia Society through educational grants for some of the organization's initiatives.

RESOURCES

Canadian Hemophilia Society
301-666 Sherbrooke West
Montreal, Quebec H3A 1E7
Tel: (514) 848-0503
Fax: (514) 848-9661
Toll-free: 1-800-668-2686
Email: chs@hemophilia.ca
Web site: http://www.hemophilia.ca

World Federation of Hemophilia
1425 René Lévesque Boulevard, West
Suite 1010
Montréal, Québec H3G 1T7
Tel: (514) 875-7944
Fax: (514) 875-8916
Email: wfh@wfh.org
Web site: www.wfh.org

More Than Medication
Web site: www.morethanmedication.ca

Pfizer is a leading biopharmaceutical firm engaged in the discovery, development and commercialization of human pharmaceuticals through recombinant DNA and other technologies.

The company has been a pioneer in the development and discovery of recombinant protein products, including coagulation factors for the treatment of hemophilia, and development of the first commercially available recombinant factor VIII and factor IX products.

By supporting research for these recombinant products, as well as providing important product and clinical trial information, Pfizer offers the hemophilia community an important resource for innovative and effective products, as well as information, education and community support.

Dedicated to advancing the care of people with hemophilia and their caregivers through advanced technologies and community-based programs, Pfizer supports hemophilia research, scientific meetings, patient advocacy organizations and provides educational materials.

For additional information, please contact your healthcare provider or Pfizer medical information at 1-800-463-6001.

Pr BeneFix® TM
Coagulation Factor IX (Recombinant)

Pfizer Rare Disease Hemophilia

MEMBER OF INNOVATIVE MEDICINES CANADA

REVIEWED BY PAAB

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