# PACKAGE LEAFLET: INFORMATION FOR THE USER

**NanoFIX 500 IU / 1000 IU, Powder and Solvent for Solution for Injection**

**Human Coagulation Factor IX**

**Read all of this leaflet carefully before you start using this medicine because it contains important information for you.**
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects , talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

**What is in this leaflet**



## 1. What NanoFIX is and what it is used for

NanoFIX belongs to a group of medicines called clotting factors and contains the human blood coagulation factor IX. This is a special protein, which increases the ability of the blood to clot.

NanoFIX is used for the treatment and prevention of bleeding in patients with bleeding disorder (haemophilia B). This is a medical condition in which bleeding can go on for longer than expected. It is due to an in-born deficiency in the amount of coagulation factor IX in the blood.

NanoFIX is supplied as a powder and solvent to prepare a solution for injection. After reconstitution, it is administered intravenously (injected into a vein).

## 2. What you need to know before you use NanoFIX

**Do not use NanoFIX:**

- if you are allergic to human blood coagulation factor IX or any of the other ingredients of this medicine (listed in section 6).

- if you suffer from heparin-induced thrombocytopenia type II, which is a fall in the number of platelets in the blood after administration of heparin. Platelets are cells in the blood that help to stop bleeding. Heparin is a medicine used to prevent blood clots.

**Warnings and precautions**

Talk to your doctor of pharmacist before using NanoFIX

- As with any medicine which contains proteins and which is administered intravenously, allergic type hypersensitivity reactions can occur. NanoFIX contains very small amounts of human proteins other than factor IX and heparin. Early signs of hypersensitivity reactions include:
  - hives
  - rash (urticaria)
  - tightness of the chest
  - wheezing
  - low blood pressure
  - acute, severe allergic reaction (anaphylaxis when any or all of the above symptoms develop rapidly and are intense)

  If these symptoms occur, stop the injection immediately and consult your doctor. In case of anaphylactic shock, he/she must start the recommended treatment as soon as possible.
- Your doctor may recommend that you consider vaccination against hepatitis A and B if you regularly / repeatedly receive human plasma-derived factor IX products.
- It is known that individuals with haemophilia B may develop inhibitors (neutralising antibodies) to factor IX, produced by the immune cells. Inhibitors may increase the risk of suffering an anaphylactic shock (severe allergic reactions). Therefore, if you suffer an allergic reaction, you should be tested for the presence of an inhibitor. Patients with factor IX inhibitors may be at higher risk of anaphylaxis if they are treated with factor IX. Your doctor may therefore decide to give the first injection of factor IX under medical supervision, where appropriate medical care for allergic reactions can be provided.
- Factor IX protein concentrates may cause an obstruction of your blood vessels with a clot. Because of this risk, which is higher in low purity products, you should be monitored for signs of the formation of blood clots after the administration of factor IX products if you:
  - have signs of fibrinolysis (blood clots which are broken down)
  - have disseminated intravascular coagulation (the widespread clotting of the blood within the blood vessels)
  - are diagnosed with liver disease
  - have documented cardiovascular risk factors
  - had surgery recently
  - are at higher risk of clot formation or of disseminated intravascular coagulation.

If any of the above conditions is true for you, your doctor will only give you NanoFIX if the benefit outweighs the risks.

- After repeated treatment with human coagulation factor IX products, patients should be monitored for the development of neutralising antibodies (inhibitors) that should be quantified in Bethesda Units (BU) using appropriate biological testing.

Virus safety of blood products

- When medicines are made from human blood or plasma, certain measures are put in place to prevent infections being passed on to patients. These include careful selection of blood and plasma donors to make sure those at risk of carrying infections are excluded, and the testing of each donation and pools of plasma for signs of virus. Manufacturers of these products also include steps in the processing of the blood or plasma that can inactivate or remove viruses. Despite these measures, when medicines prepared from human blood or plasma are administered, the possibility of passing on infection cannot be totally excluded. This also applies to any unknown or emerging viruses or other types of infections.
- The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus, and for the non-enveloped hepatitis A virus. The measures taken may be of limited value against non-enveloped viruses such as parvovirus B19. Parvovirus B19 infection may be serious for pregnant women (fetal infection) and for individuals whose immune system is depressed or who have some types of anaemia (e.g. sickle cell disease or haemolytic anaemia).

It is strongly recommended that every time you receive a dose of NanoFIX the name and batch number of the product are recorded in order to maintain a record of the batches used.

**Children**

If NanoFIX is given to a new-born infant, the child must be closely monitored for signs of disseminated intravascular coagulation.

**Other medicines and NanoFIX**

- As far as is known, human blood coagulation factor IX products do not interact with any other medicinal products.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

**Pregnancy and breast-feeding**

There is no experience on the use of factor IX during pregnancy and breast-feeding. Therefore, factor IX should be used during pregnancy and breast feeding only if it is clearly indicated.

Ask your doctor or pharmacist for advice before taking any medicine.

**Driving and using machines**

No effects on ability to drive and use machines have been observed.

**NanoFIX contains sodium**

This medicinal product contains up to 69 mg sodium (main component of cooking / table salt) for 1 vial NanoFIX 500 IU equivalent to 3.45% of the recommended maximum daily dietary intake of sodium for an adult and

up to 138 mg sodium for 1 vial NanoFIX 1000 IU equivalent to 6.9% of the recommended maximum daily dietary intake of sodium for an adult.

You should take this into consideration if you are on a controlled sodium diet.

## 3. How to use NanoFIX

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.
NanoFIX should be administered intravenously (injected into a vein) after being reconstituted with the supplied solvent.
Only use the infusion set provided. The use of other injection/infusion equipment can cause additional risks and treatment failure.
Treatment should be started under the supervision of a physician experienced in the treatment of haemophilia. How much NanoFIX you should use and how long the substitution therapy must be continued depends on the severity of your factor IX deficiency. It also depends on the site and extent of the bleeding, as well as on your clinical condition.

**Dosage calculation:**

Your doctor will tell you how often and how much NanoFIX you need to inject.

The dosage of factor IX is expressed in International Units (IU). Factor IX activity in the plasma refers to the amount of Factor IX present in the plasma. It is expressed either as a percentage (relative to normal human blood plasma) or in International Units (relative to an international standard for factor IX in blood plasma).

One International Unit (IU) of factor IX activity is equivalent to the amount of factor IX in one ml of normal human blood plasma. The calculation of the required dosage of factor IX is based on the finding that 1 IU of Factor IX per kg body weight raises the blood plasma factor IX activity by 1% of normal activity. To calculate the dosage you require, the level of factor IX activity in your blood plasma is measured. This will indicate by how much the activity needs to be increased.

The dosage required is calculated using the following formula:

**Required units = body weight (kg) x desired factor IX increase (%) (IU/dl) x 0.8**

The size of your dose and how often it must be administered will depend on how you respond to the medicine and will be decided by your doctor. Factor IX products rarely require to be administered more than once daily.

Your response to factor IX products may vary. Your factor IX levels should therefore be measured during the treatment to calculate the correct dosage and frequency of infusion. Especially during surgeries, your doctor will use blood tests (plasma factor IX activity) to monitor the substitution therapy closely.

**Prevention of bleeding:**

If you suffer from severe haemophilia B you should inject 20 to 40 IU of factor IX per kg body weight (BW). You should administer this dosage twice weekly for long-term prevention. Your dose should be adjusted according to your response. In some cases, especially in younger patients, shorter dosage intervals or higher doses may be necessary.

**Use in children**

In the study conducted in children under 6 years of age, the median dose administered per exposure day was 40 IU/kg BW.

**If your bleeding cannot be stopped due to inhibitors:**
If the expected activity of factor IX is not attained after an injection, or bleeding does not stop after the correct dose, you should notify your doctor. He will examine your blood plasma to see if you have developed inhibitors (antibodies) against the factor IX protein. These inhibitors may reduce the activity of factor IX. In this case it may become necessary to choose a different treatment. Your doctor will discuss this with you and recommend further treatment if necessary
.

**If you use more NanoFIX than you should**

No symptoms of overdose with human coagulation factor IX have been reported. However, the recommend dose should not be exceeded.

**For „Instructions for Home Treatment“, please refer to the carton for the equipment package.**

## 4. Possible side effects

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

- Hypersensitivity or allergic reactions have been observed infrequently in patients treated with factor IX containing products. These can include:
  - involuntary contraction of the blood vessels (spasms) with swelling of the face, mouth and throat
  - burning and stinging at the infusion site
  - chills
  - flushing
  - rash
  - headache
  - hives
  - low blood pressure
  - tiredness

- feeling sick
- restlessness
- rapid heart beat
- tightness of the chest
- feeling of pins and needles
- vomiting
- wheezing.

In some cases, these allergic reactions may lead to a severe reaction called anaphylaxis, which may include shock. These reactions are mostly associated with the development of factor IX inhibitors. If you suffer from one of the above mentioned symptoms, please inform your doctor.

- If you suffer from haemophilia B you may develop neutralising antibodies (inhibitors) to factor IX. These antibodies can stop your medicine working properly. Your doctor will discuss this with you and recommend further treatment if necessary.
  A study in 25 children with Haemophilia B was conducted, thereof 6 patients were previously untreated. No inhibitor was observed during the study. The tolerability of all injections was rated as “very good” or “good”.
- Some haemophilia B patients with factor IX inhibitors with immune tolerance therapy and a history of allergic reactions developed nephrotic syndrome (a severe kidney condition).
- Fever may occur in rare cases.
- Low purity factor IX products may in rare cases cause a blood clot to form within a blood vessel. This may lead to any of the following complications:
  - heart attack
  - widespread clotting in the blood vessels (disseminated intravascular coagulation)
  - Blood clots in the veins (venous thrombosis)
  - Blood clots in the lungs (pulmonary embolism).

  These side effects are more common if you use factor IX products of low purity and only occur rarely if you use products of high purity such as NanoFIX.
- The heparin in the preparation may cause a sudden fall in the number of platelets in the blood to below 100,000 per microlitre or less than 50% of the starting count. This is an allergic reaction called “heparin-induced thrombocytopenia type II”. In rare cases in patients not previously hypersensitive to heparin, this fall in the number of platelets can occur 6-14 days after the start of treatment. In patients with a previous heparin hypersensitivity, this alteration may develop within a few hours of starting treatment. This severe form of blood platelet reduction may be accompanied by, or result in:
  - blood clots in the arteries and veins
  - obstruction of a blood vessel by a clot from another area
  - a severe blood clotting disorder called consumptive coagulopathy
  - skin gangrene in the area of injection
  - flea bite-like bleeding

- purple bruising
- tarry stools.

**If you observe these allergic reactions, immediately stop injections with NanoFIX and do not use medicinal products containing heparin in the future.** Because of this rare effect on the blood platelets, your doctor should closely monitor the blood platelet count, especially at the start of treatment.

For safety with respect to transmissible agents, see section 2.

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any side effects not listed in this leaflet.

**Reporting of side effects**
If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system. By reporting side effects you can help provide more information on the safety of this medicine.

HPRA Pharmacovigilance
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail:medsafety@hpra.ie

## 5. How to store NanoFIX

Keep this medicine out of the sight and reach of children.

Do not store above 25°C.

Do not freeze.

Keep the vial in the outer carton in order to protect from light.
Do not use this medicine after the expiry date which is stated on the label and on the carton. The expiry date refers to the last day of that month.

It is recommended to use the reconstituted product immediately, but at least within 8 hours stored at room temperature (25°C).

Use NanoFIX on one occasion only.

Do not use this medicine if you notice turbid or incompletely dissolved solutions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

## 6. Contents of the pack and other information

**What NanoFIX contains**
The **active substance** is the human blood coagulation factor IX.

The **other ingredients** are heparin, sodium chloride, sodium citrate, arginine hydrochloride and lysine hydrochloride.

**What NanoFIX looks like and contents of the pack**
NanoFIX comes in 2 pack sizes with the following strengths:

- NanoFIX 500 IU is presented as a powder and solvent for solution for injection containing nominally 500 IU human coagulation factor IX per vial.

  The product contains approximately 100 IU/ml human coagulation factor IX when reconstituted with 5 ml water for injections.
- NanoFIX 1000 IU is presented as a powder and solvent for solution for injection containing nominally 1000 IU human coagulation factor IX per vial.

  The product contains approximately 100 IU/ml human coagulation factor IX when reconstituted with 10 ml water for injections.

NanoFIX is produced from plasma of human donors.

The potency (IU) is determined using the European Pharmacopoeia one stage clotting assay, in comparison with an international standard from the World Health Organisation (WHO). The specific activity of NanoFIX is approximately 100 IU/mg protein.

**Description of the package:**

NanoFIX is sold in a combination package consisting of two cartons held together with a plastic film:

One carton contains 1 vial with powder for solution for injection and the package leaflet.

The other carton contains the vial with the solvent (water for injections); 5 ml for NanoFIX 500 IU and 10 ml for NanoFIX 1000 IU.

This package also contains the following medical devices:
- 1 equipment pack for intravenous injection (1 transfer set, 1 infusion set, 1 disposable syringe)
- 2 alcohol swabs

**Marketing Authorisation Holder and Manufacturer**

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

Octapharma (IP) SPRL
Allée de la Recherche 65
1070 Anderlecht
Belgium

Manufacturer: Octapharma Pharmazeutika Produktionsges.m.b.H.
Oberlaaer Strasse 235
A-1100 Vienna
Austria

or

Octapharma S.A.S.
70-72 Rue du Maréchal Foch
67380 Lingolsheim
France

**This leaflet was last revised in 11/2020.**

**Instructions for Home Treatment**

- **Please read all the instructions and follow them carefully!**
- **During the procedure described below, sterility must be maintained!**
- **Do not use OCTANINE after the expiry date given on the label and carton.**
- **Reconstituted medicinal product should be inspected visually for particulate matter and discoloration prior to administration.**
- **The solution should be clear or slightly opalescent. Do not use solutions that are cloudy or have deposits.**
- **Use the prepared solution immediately, to prevent microbial contamination.**
- **Only use the infusion set provided. The use of other injection/infusion equipment can cause additional risks and treatment failure.**

**<u>Instructions for preparing the solution:</u>**

**1.** Do not use the product directly from the refrigerator. Allow the solvent and the powder in the closed vials to reach room temperature.

**2.** Remove the flip off caps from both vials and clean the rubber stoppers with one of the provided alcohol swabs.

**3.** The transfer set is depicted in Fig. 1. Place the solvent vial on an even surface and hold it firmly. Take the transfer set and turn it upside down. Place the blue part of the transfer set on top of the solvent vial and press firmly down until it snaps (Fig. 2 + 3). Do not twist while attaching.

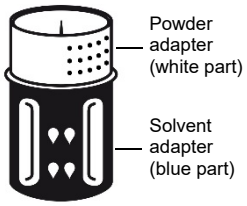


Fig. 1


Fig. 2


Fig. 3

**4.** Place the powder vial on an even surface and hold it firmly. Take the solvent vial with the attached transfer set and turn it upside down. Place the white part on top of the powder vial and press firmly down until it snaps (Fig. 4). Do not twist while attaching. The solvent flows automatically into the powder vial.

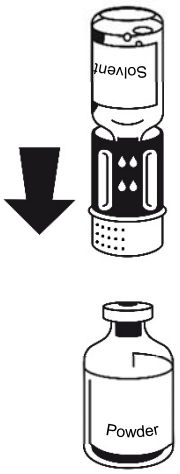


Fig. 4

**5.** With both vials still attached, gently swirl the powder vial until the product is dissolved.
The dissolving is completed in less than 10 minutes at room temperature. Slight foaming might occur during preparation. Unscrew the transfer set into two parts (Fig. 5). Foaming will disappear.

Dispose the empty solvent vial together with the blue part of the transfer set.

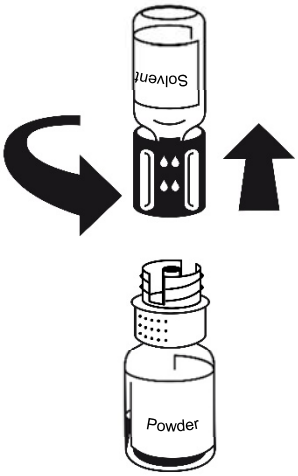


Fig. 5

**Instructions for injection:**

As a precaution, your pulse rate should be taken before and during the injection. If a marked increase in your pulse rate occurs, reduce the injection speed or interrupt the administration for a short time.

1. Attach the syringe to the white part of the transfer set. Turn the vial upside down and draw the solution into the syringe (Fig. 6).
   The solution should be clear or slightly opalescent.
   Once the solution has been transferred, firmly hold the plunger of the syringe (keeping it facing down) and remove the syringe from the transfer set (Fig. 7).
   Dispose the empty vial together with the white part of the transfer set.

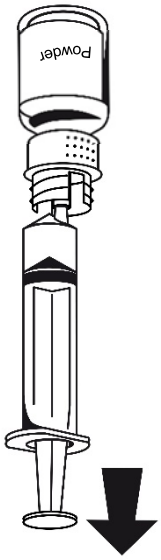


Fig. 6

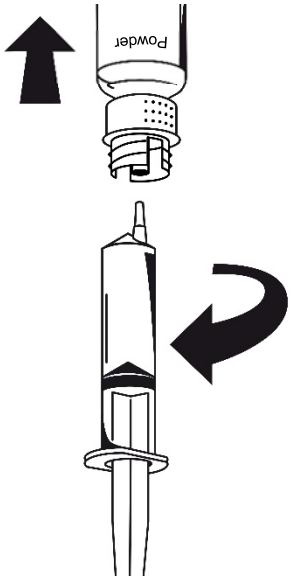


Fig. 7

2. Clean the chosen injection site with one of the provided alcohol swabs.

3. Attach the provided infusion set to the syringe.

4. Insert the injection needle into the chosen vein. If you have used a tourniquet to make the vein easier to see, this tourniquet should be released before you start injecting OCTANINE.
   No blood must flow into the syringe due to the risk of formation of fibrin clots.

5. Inject the solution into the vein at a slow speed, not faster than 2-3 ml per minute.

If you use more than one vial of OCTANINE powder for one treatment, you may use the same injection needle and syringe again. The transfer set is for single use only.

Any unused product or waste material should be disposed of in accordance with local requirements.