Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

Benefix® 250 IU
Benefix® 500 IU
Benefix® 1000 IU
Benefix® 2000 IU

Powder and diluent for solution for intravenous (IV) injection

Each vial contains:
Recombinant coagulation factor IX 250IU, 500IU, 1000IU, 2000IU

For a list of inactive ingredients and allergens, see section 6 "Further information".

Read the entire leaflet carefully before using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

1. WHAT IS THIS MEDICINE INTENDED FOR?

Benefix® is indicated for prevention and reduction of the rate of bleeding episodes in patients with hemophilia B (congenital factor IX deficiency or Christmas disease), including control of bleeding in surgical settings, in previously treated patients and previously untreated patients.

Benefix® is not indicated for the treatment of other factor deficiencies (factors II, VII, X), not for treatment of hemophilia A patients with inhibitors to factor VIII, not for reversal of coumarin (Warfarin)-induced anticoagulation and not for treatment of bleeding due to low levels of liver-dependent coagulation factors.

Therapeutic group: coagulation factor.

2. BEFORE USING THIS MEDICINE

Do not use this medicine if: you had a life-threatening, immediate hypersensitivity, including anaphylaxis, to the active ingredient or to any of the other ingredients in this medicine, listed in section 6, including sensitivity to hamster protein.

Special warnings regarding use of the medicine

Call your doctor right away if bleeding is not controlled after injecting the medicine.

Before treatment with Benefix®, tell your doctor if:
- you have any allergies, including allergies to hamsters.
- you are pregnant or planning to become pregnant.
- are breastfeeding or planning to breastfeed.

Children and adolescents
Benefix® can be used in children and adolescents of all ages.

Tests and follow up
Your doctor may perform various tests to examine the activity of the medicine.

Drug interactions
If you are taking or have recently taken, other medicines, including nonprescription medicines and dietary supplements, tell your doctor or pharmacist.

Pregnancy, breastfeeding, and fertility
Inform your doctor if you are pregnant, think you may be pregnant or are planning to become pregnant. It is not known whether Benefix® may harm the fetus. Consult your doctor before using Benefix®.

Inform your doctor if you are breastfeeding or are planning to breastfeed. It is not known whether Benefix® passes into breast milk or whether it may harm your baby.

3. HOW TO USE THIS MEDICINE?

Benefix® is marketed as a powder and diluent in a prefilled syringe. Before the injection, you must dilute the powder with the diluent provided in the package. Benefix® is administered by intravenous injection. Do not swallow.

Always use this preparation according to your doctor's instructions.

Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.

The dosage and treatment regimen will be determined by your doctor only.

Do not exceed the recommended dose.

If you have taken an overdose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

Adhere to the treatment as recommended by your doctor.

If you forget to take the medicine at the scheduled time, contact your doctor.

Even if your health improves, do not stop taking this medicine without consulting your doctor.

Do not take medicines in the dark! Check the label and dose <u>each time</u> you take a medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Benefix® may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

An allergic reaction may occur with Benefix® treatment. Contact your doctor or proceed to the emergency room right away if you have any of the following symptoms: wheezing (during breathing), difficulty breathing, chest tightness, turning blue (blue lips and gums), fast heartbeat, swelling of the face, faintness, rash, hives.

In addition, your body may produce antibodies against the preparation, which may impair the efficacy of the preparation.

Additional side effects include:
Common side effects (occur in 1-10 of 100 users):
fever, cough, nausea, injection site reaction, injection site pain, headache, dizziness and rash.

Benefix® may increase the risk of thromboembolism (abnormal blood clots) in your body if you have risk factors for developing blood clots, including an infusion catheter through which Benefix® is administered by continuous infusion.

There have been reports of severe blood clotting events, including life-threatening blood clots in ill neonates receiving Benefix® by continuous infusion through a catheter. The efficacy and safety of Benefix® administered by continuous infusion have not been established.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects or by using the link: https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?

- Prevent poisoning! This and any other medicine should be kept in a closed place, out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.

<u>Before reconstitution</u>: Store below 30°C. **Do not freeze.**

<u>After reconstitution</u>: Use within 3 hours.

6.FURTHER INFORMATION

In addition to the active ingredient, this medicine also contains:
glycine, sucrose, histidine, polysorbate 80, HCl, sodium chloride.
The syringe contains: 0.234% sodium chloride solution.

What the medicine looks like and contents of the pack:
Benefix® is marketed as a white powder in a vial and a clear diluent in a prefilled syringe.

Each package contains:
1 powder vial with coagulation factor IX (recombinant) 250, 500, 1000 or 2000IU
1 prefilled syringe with 5 ml diluent (0.234% sodium chloride solution)
1 sterile vial adapter.
1 sterile infusion set.
2 alcohol swabs.
1 adhesive bandage.
1 gauze pad.

Not all medicine strengths may be marketed.

Registration holder and address:
Pfizer Pharmaceuticals Israel Ltd., 9 Shenkar St., Herzliya Pituach 46725

Manufacturer's name and address:
Wyeth Farma S.A, Madrid, Spain

Registration number of the medicine in the National Drug Registry of the Ministry of Health:
Benefix® 250 IU: 120-55-30121
Benefix® 500 IU: 120-56-30122
Benefix® 1000 IU: 120-57-30123
Benefix® 2000 IU: 142-66-31926

<u>Instructions for use</u>

Please read the entire instructions before using Benefix®. Follow these instructions step by step. Please do not use the preparation unless you have been instructed by healthcare professionals.

If there is anything you do not understand or cannot perform, or if you have any questions about the dose or treatment with Benefix®, contact the healthcare professionals.

<u>Reconstitution</u>

Wash your hands with soap and water before using Benefix®.

Try to perform the reconstitution in a clean environment.

Once you open the vial, you should complete the reconstitution as soon as possible.

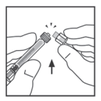
If you use more than one vial of Benefix®, reconstitute each vial according to steps 1 through 13.

1. If the medicine has been stored in the refrigerator, let the vial and the pre-filled diluent syringe reach room temperature.
2. Remove the plastic cap from the vial to expose the rubber stopper of the vial.

3. Wipe the top of the vial with the alcohol swab provided in the package and allow to dry. After cleaning, do not touch the top of the vial or allow it to touch any surface or object.
4. Peel back the cover from the vial adapter. **Do not remove the adapter from the package.**
5. Place the vial on a flat surface. While holding the adapter in the package, place the vial adapter over the vial. Press down firmly on the adapter package until the adapter snaps into place on top of the vial, with the adapter spikes penetrating the vial stopper.

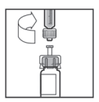
6. Grasp the plunger rod as shown in the picture. Do not touch the shaft itself. Attach the threaded end of the plunger rod to the diluent syringe plunger by pushing and turning firmly.

7. Break off the plastic cap from the syringe. Do not touch the cap or the syringe tip.

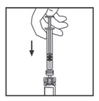


8. Lift the package away from the adapter and discard the package.

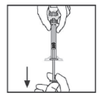
9. Place the vial on a flat surface. Connect the diluent syringe to the vial adapter by inserting the tip of the syringe into the adapter opening while firmly pushing and turning the syringe clockwise until the connection is secured.



10. Slowly push the plunger rod to inject all the diluent into the preparation vial.



11. With the syringe still connected to the adapter, **gently** swirl the contents of the vial until all the powder is dissolved.
    Look at the solution before infusing it. The solution should be clear and colorless. If it is not, discard the vial and use a new preparation kit.
12. Make sure the syringe plunger rod is still pressed down, turn over the vial and draw the solution into the syringe. Turn the syringe upward and remove any air bubbles by gently tapping the syringe with your fingers. If you use more than one vial of the preparation, remove the diluent syringe from the vial adapter and leave the vial adapter attached to the vial. Quickly attach a large syringe and draw the solution as explained in the previous sections. Repeat this procedure with each vial in turn. Do not detach the diluent syringe or the large luer lock syringe until you are ready to attach the large luer lock syringe to the next vial adapter.



13. Remove the syringe from the vial adapter by gently pulling and turning the syringe counter-clockwise. Throw away the vial with the adapter attached. If you are not using the solution right away, you should cover the syringe with the cap. Do not touch the syringe tip or the inside of the cap.

    The preparation should be infused within 3 hours after reconstitution. The reconstituted solution may be stored at room temperature prior to infusion.

<u>Infusion</u>

Do not infuse the preparation by continuous infusion.

Your attending doctor or nurse will show and teach you how to infuse Benefix®. Once you learn how to self-infuse, you can follow the instructions in this insert.

1. Attach the syringe to the sterile infusion set provided in the package.
2. Apply a tourniquet and prepare the injection site by wiping the skin well with an alcohol swabs provided in the preparation package.

3. Insert the butterfly needle of the infusion set tubing into your vein as instructed by your doctor or nurse. Remove the tourniquet. Infuse the preparation over several minutes. Your comfort level should determine the rate of infusion.

Clumping of red blood cells in the syringe during infusion of the preparation has been reported. No adverse events have been reported in association with this observation. To minimize red blood cell clumping, it is important to limit the amount of blood entering the tubing. Blood should not enter the syringe. If you observe red blood cell clumping in the tubing or syringe, discard the entire kit (tubing, syringe with the preparation and the infusion set) and use a new preparation kit.

4. After infusing the preparation into the vein, discard the syringe and the infusion set. The amount of medicine left in the infusion set will not affect your treatment. Dispose of the needle, vial and infusion set in an appropriate container.
   It is recommended to record the lot number appearing on the vial every time you use the preparation.

Revised in 12/2020.