Package leaflet: Information for the user

FIBRYGA 2 g powder and solvent for solution for injection / infusion
Human fibrinogen

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 or pharmacist.
- 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet
1. What FIBRYGA is and what it is used for
2. What you need to know before you use FIBRYGA
3. How to use FIBRYGA
4. Possible side effects
5. How to store FIBRYGA
6. Contents of the pack and other information

1. What FIBRYGA is and what it is used for

What FIBRYGA is

FIBRYGA contains human fibrinogen which is a protein important for blood clotting (coagulation). Lack of fibrinogen means that the blood does not clot as well as it should, which results in an increased tendency to bleed. The replacement of human fibrinogen with FIBRYGA will correct the coagulation defect.

What FIBRYGA is used for

FIBRYGA is used for:

- treatment of bleeding episodes and prophylaxis for surgery in patients with congenital lack of fibrinogen (hypo- or afibrinogenaemia) with a bleeding tendency.
- fibrinogen supplementation in patients with uncontrolled severe bleeding accompanied by acquired lack of fibrinogen during surgery.

2. What you need to know before you use FIBRYGA

Do NOT use FIBRYGA:

- if you are allergic to human fibrinogen or any of the other ingredients of this medicine (listed in section 6).
- if you have experienced allergic reactions to FIBRYGA in the past.

Please inform your doctor if you are allergic to any medicine.

Warnings and precautions

Talk to your doctor or pharmacist before using FIBRYGA.

Risk of clots in blood vessels

Your doctor should evaluate the benefits of this medicine against the risk of clots in blood vessels, in particular if:

- you have received high dose or repeated dosing of this medicine
- you have had a heart attack (history of coronary heart disease or myocardial infarction)
- you have liver disease
- you have just had surgery (patients postoperatively)
- you are having surgery (patients perioperatively)
- in newborn infants (neonates)
- you are likely to suffer from clots or clotting problems in blood vessels (patients at risk of thromboembolic events or disseminated intravascular coagulation).

Your doctor may ask you to have additional clotting tests done in order to monitor the risk.

Allergic or anaphylactic-type reactions

Any medicine, such as FIBRYGA, which is prepared from human blood (containing proteins) and which is injected into a vein (administered intravenously) can cause allergic reactions. If you have experienced allergic reactions to FIBRYGA in the past, your doctor will advise you whether anti-allergy medication is needed.

Your doctor will explain to you the warning signs of allergic or anaphylactic-type reactions.

Please pay attention to early signs of allergic reactions (hypersensitivity), such as:

- hives
- skin rash
- tightness of the chest
- wheezing
- low blood pressure,
- or anaphylaxis (when any or all of the above symptoms develop rapidly and are intense).

If they occur, the injection / infusion of FIBRYGA should be stopped immediately (i.e. discontinue injection).

Virus safety

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
- the testing of each donation and pools of plasma for signs of virus/infections
- the inclusion of 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 (infection of the unborn baby) and for individuals whose immune system is depressed or who have some types of anaemia (e.g. sickle cell disease or abnormal breakdown of red blood cells).

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

Your doctor may recommend that you consider vaccination against hepatitis A and B if you regularly/repeatedly receive human plasma-derived fibrinogen products.

Children and adolescents

There are no specific or additional warnings or precautions applicable for children and adolescents.

Other medicines and FIBRYGA

Tell your doctor or pharmacist if you are using, have recently used, or might use any other medicines. FIBRYGA must not be mixed with other medicines except those mentioned in section *"The following information is intended for healthcare professionals only / Reconstitution"*.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. This product should only be used during pregnancy or breast-feeding after consultation with your doctor or pharmacist.

Driving and using machines

FIBRYGA has no influence on the ability to drive and use machines.

FIBRYGA contains sodium

This medicine contains up to 264 mg sodium (main component of cooking/table salt) in each bottle. This is equivalent to 13.2% of the recommended maximum daily dietary intake of sodium for an adult. Please take this into account if you are on a controlled sodium diet.

3. How to use FIBRYGA

Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

FIBRYGA is given as an intravenous infusion (infusion into a vein) by healthcare personnel.

The dose and dosage regimen depends on:

- your weight
- the severity of your disease
- the location of the bleeding or
- the nature of your operation and
- your health status

Use in children and adolescents

The administration of FIBRYGA in children and adolescents (intravenously) does not differ from the administration in adults.

If you use more FIBRYGA than you should

To avoid the risk of overdose, your doctor will perform regular blood tests to measure your fibrinogen level.

In case of overdose, the risk of abnormal clots in your blood vessels may become increased.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

Method of administration

This medicine should be injected or infused into the veins after reconstitution with the supplied solvent. If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

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

Please contact your doctor immediately:

- **if any of the side effects occur**
- **if you notice any side effects not listed in this leaflet**

The following side effects have been reported for FIBRYGA and other fibrinogen products (the frequency of the listed side effects is not known):

- Allergic or anaphylactic-type reactions: skin reactions such as skin rash or reddening of the skin (see section 2 “Warnings and precautions”)
- Cardiovascular: inflammation of veins and formation of blood clots (see section 2 “Warnings and precautions”)
- increase in body temperature

If you experience any of the symptoms above, contact your doctor as soon as possible.

Reporting of side effects

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

5. How to store FIBRYGA

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

Do not use this medicine after the expiry date which is stated on the label and carton. The expiry date refers to the last day of that month.

Do not store above 25°C. Do not freeze. Keep the bottle in the outer carton to protect from light.

Chemical and physical in-use stability has been demonstrated for 24 hours at room temperature (15 – 25°C). From a microbiological point of view, unless the method of reconstitution precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user. Do not refrigerate or freeze.

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 FIBRYGA contains

- The active substance is human fibrinogen.
- FIBRYGA contains 2 g human fibrinogen per bottle or 20 mg/mL human fibrinogen after reconstitution with the supplied solvent (100 mL water for injection).
- The other ingredients are arginine hydrochloride, glycine, sodium chloride and sodium citrate dihydrate.

What FIBRYGA looks like and contents of the pack

FIBRYGA is presented as a powder and solvent for solution for injection/ infusion and is available in glass bottles.

The powder is white or pale yellow and hygroscopic, also appearing as a friable mass.

The solvent is a clear and colourless liquid.

The reconstituted solution is almost colourless and slightly opalescent.

FIBRYGA is sold in one carton containing:
- 1 bottle with powder for solution for injection/ infusion
- 1 vial with solvent (water for injections)
- 1 nextaro transfer device

Marketing Authorisation Holder

[To be completed nationally]

Manufacturer

Octapharma AB,
Lars Forssells gata 23, 112 75 Stockholm, Sweden

This medicinal product is authorised in the Member States of the European Economic Area under the following names:

Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Norway, Poland, Portugal, Romania, Slovakia, Spain, Sweden, The Netherlands. Fibryga®

Slovenia. Fibrema®

This leaflet was last revised in

[To be completed nationally]

The following information is intended for healthcare professionals only:

Posology

The dosage and duration of the substitution therapy depend on the severity of the disorder, location and extent of bleeding and the patient's clinical condition.

The (functional) fibrinogen level should be determined in order to calculate individual dosage and

the amount and frequency of administration should be determined on an individual patient basis by regular measurement of plasma fibrinogen level and continuous monitoring of the clinical condition of the patient and other replacement therapies used.

In case of major surgical intervention, precise monitoring of replacement therapy by coagulation assays is essential.

1. Prophylaxis in patients with congenital hypo- or afibrinogenaemia and known bleeding tendency.

To prevent excessive bleeding during surgical procedures, prophylactic treatment is recommended to raise fibrinogen levels to 1 g/L and maintain fibrinogen at this level until haemostasis is secured and above 0.5 g/L until wound healing is complete.

In case of surgical procedure or treatment of a bleeding episode, the dose should be calculated as follows:

$$\text{Dose (mg/kg body weight)} = \frac{\text{[Target level (g/L) - measured level (g/L)]}}{\text{0.018 (g/L per mg/kg body weight)}}$$

Subsequent posology (doses and frequency of injections) should be adapted based on the patient's clinical status and laboratory results.

The biological half-life of fibrinogen is 3 – 4 days. Thus, in the absence of consumption, repeated treatment with human fibrinogen is not usually required. Given the accumulation that occurs in case of repeated administration for a prophylactic use, the dose and the frequency should be determined according to the therapeutic goals of the physician for a given patient.

Paediatric population

In case of surgical procedure or treatment of a bleeding episode, the dose in adolescents should be calculated according to the formula described for adults above, while the dose in children <12 years of age should be calculated as follows:

$$\text{Dose (mg/kg body weight)} = \frac{\text{[Target level (g/L) - measured level (g/L)]}}{\text{0.014 (g/L per mg/kg body weight)}}$$

Subsequent posology should be adapted based on the patient's clinical status and laboratory results.

Elderly patients

Clinical studies of FIBRYGA did not include patients aged 65 years and over to provide conclusive evidence as to whether or not they respond differently than younger patients.

2. Treatment of bleeding

Bleeding in patients with congenital hypo- or afibrinogenaemia

Bleeding episodes should be treated according to the formulas above for adults/adolescents and children, respectively, to achieve a recommended target fibrinogen plasma level of 1 g/L. This level should be maintained until haemostasis is secured.

Bleeding in patients with acquired fibrinogen deficiency

Adults

Generally, 1-2 g is administered initially with subsequent infusions as required. In case of severe haemorrhage e.g. major surgery, larger amounts (4-8 g) of fibrinogen may be required.

Paediatric population

The dosage should be determined according to the body weight and clinical need but is usually 20-30 mg/kg.

Instructions for Preparation and Administration

General Instructions

- The reconstituted solution should be almost colourless and slightly opalescent. Do not use solutions that are cloudy or have deposits.
- FIBRYGA is for single use only. Do not re-use any of the components.
- Chemical and physical in-use stability has been demonstrated for 24 hours at room temperature (15 – 25°C). From a microbiological point of view, unless the method of reconstitution precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user. Do not refrigerate or freeze.

Reconstitution

1. Ensure that the powder (FIBRYGA) bottle and solvent vial are at room temperature. This temperature should be maintained during reconstitution. If a water bath is used for warming, care must be taken to avoid water coming into contact with the rubber stoppers or the flip caps of the containers. The temperature of the water bath should not exceed +37°C.
2. Remove the flip caps from the powder (FIBRYGA) bottle and the solvent vial to expose the central portion of the infusion stopper. Clean the rubber stoppers with an alcohol swab and allow the rubber stoppers to dry.
3. Open the transfer device (nextaro) package by peeling off the lid (Fig. 1). To maintain sterility, do not remove the transfer device from the clear blister package. Do not touch the spike.

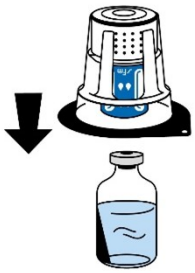


Transfer device

Fig. 1

4. Place the solvent vial on an even, clean surface and hold it firmly. Without removing the blister package, place the blue part of the transfer device on top of the solvent vial. Press straight and firmly down until it snaps into place (Fig. 2). Do not twist while attaching.

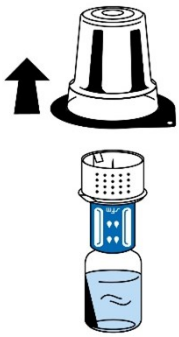
   Note:
   The transfer device must be attached to the solvent vial first and then to the lyophilized powder bottle. Otherwise, loss of vacuum occurs, and transfer of the solvent does not take place.



Solvent vial

Fig. 2

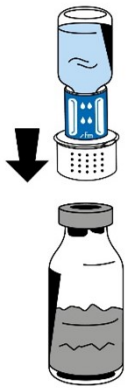
5. While holding onto the solvent vial, carefully remove the blister package from the transfer device (nextaro) by pulling vertically upwards. Make sure to leave the transfer device attached firmly to the solvent vial (Fig. 3).



Solvent vial

Fig. 3

6. Place the powder (FIBRYGA) bottle on an even, clean surface and hold it firmly. Take the solvent vial with the attached transfer device and turn it upside down. Place the white part of the transfer device connector on top of the powder (FIBRYGA) bottle and press firmly down until it snaps into place (Fig. 4). Do not twist while attaching. The solvent will flow automatically into the powder (FIBRYGA) bottle.



Solvent vial

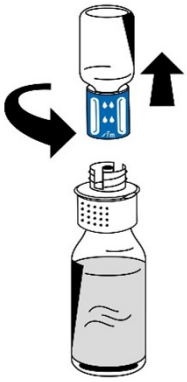
FIBRYGA bottle

Fig. 4

7. With the solvent vial still attached, gently swirl the FIBRYGA bottle until the powder is fully dissolved. To avoid foam formation, do not shake the bottle. The powder should be dissolved completely within approx. 5-10 minutes. It should not take longer than 20 minutes to dissolve the powder. If the powder is not dissolved within 20 minutes the product should be discarded.

8. On the rare occasion of un-reconstituted powder observed floating during the transfer of WFI, or the reconstitution time being unexpectedly prolonged, the dissolution process can be promoted by more rigorous horizontal agitation of the vial.

9. After reconstitution is complete unscrew the transfer device (blue part) counterclockwise into two parts (Fig. 5). Do not touch the Luer lock connector on the white part of the transfer device.



Empty Solvent vial

Reconstituted FIBRYGA bottle

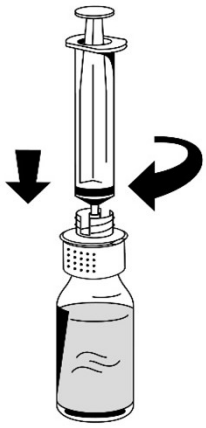
Fig. 5

10. Discard the empty solvent vial together with the blue part of the transfer device.

Administration

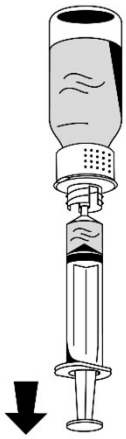
1. Carefully attach a syringe to the Luer lock connector on the white part of the transfer device (Fig. 6).

2. Turn the FIBRYGA bottle upside down and draw the solution into the syringe (Fig. 7).



Reconstituted
FIBRYGA
bottle

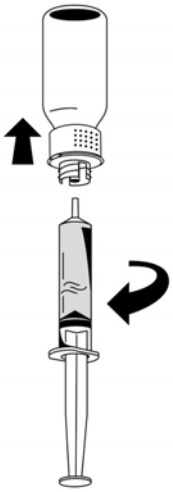
Fig. 6



Reconstituted
FIBRYGA
bottle

Fig. 7

3. Once the solution has been transferred, firmly hold the barrel of the syringe (keeping the syringe plunger facing down) and remove the syringe from the transfer device (Fig. 8).



Empty
FIBRYGA bottle

Fig. 8

4. Dispose of the white part of the transfer device together with the empty FIBRYGA bottle.

A standard infusion set is recommended for intravenous application of the reconstituted solution at room temperature.

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

Method of administration

Intravenous infusion or injection.

FIBRYGA should be administered slowly intravenously at a recommended maximum rate of 5 mL per minute for patients with congenital hypo- or afibrinogenaemia and at a recommended maximum rate of 10 mL per minute for patients with acquired fibrinogen deficiency.

Incompatibilities

This medicinal product must not be mixed with other medicinal products.