Package leaflet: Information for the user

FibCLOT 1.5 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, 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 FIBCLOT IS AND WHAT IT IS USED FOR

What FibCLOT is
It is a medicine which belongs to the class of antihaemorrhagics. The active substance is human fibrinogen, a protein which is naturally present in the body. The role of this protein is to ensure normal coagulation of the blood and to prevent that bleeding lasts too long.

What FibCLOT is used for
It is used in all age groups to compensate for the lack of human fibrinogen and, thus, prevent and treat bleeding (haemorrhages) in patients with congenital fibrinogen deficiency.
Congenital fibrinogen deficiency is a hereditary disease characterised by a level less than the normal value or an absence of a protein called fibrinogen. This lack may lead to prolonged bleedings.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE FIBCLOT

Do not use FibCLOT
If you are allergic to the active substance (human fibrinogen) or any of the other ingredients of this medicine (listed in section 6. "Contents of the pack and other information").
Please inform your doctor if your are allergic to any medicine.

Warnings and precautions:
Talk to your doctor, pharmacist or nurse before using FibCLOT.

Risk of blood clots
With high dose or repeating dosing, this medicine may increase the risk of blood clots in blood vessels.
As a consequence, your doctor should evaluate the benefits of this medicine against the risk of blood clots, particularly:
- If you have had a heart attack (history of coronary heart disease or myocardial infarction).
- If you have a liver disease.
- If you have just had surgery
- If you will be having surgery soon
- In newborn infants (neonates).
- If you are more likely to have blood clots than normal.

Your doctor may also ask you to perform additional tests in order to monitor this risk.

Risk of allergies
Your doctor will inform you of the warning signs of an allergic reaction (see section 4. "Possible side effects"). If one of these effects does occur, **this medicine should be stopped immediately**.

Virus safety
This medicine is manufactured from human plasma (the liquid part of blood).
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 the 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 or AIDS virus), 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 (foetal infection) and for individuals whose immune system is depressed or who have some types of anaemia (*e.g.* sickle cell disease or haemolytic anaemia).

Your doctor may recommend that you consider vaccination against hepatitis A and B if you regularly/repeatedly receive human plasma-derived products.
It is strongly recommended that every time you receive a dose of this medicine, the name and batch number of the medicine are recorded in order to maintain a record of the batches used.

Children and adolescents
Same warnings and precaution apply to children and adolescents.

Other medicines and FibCLOT
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines, including medicines obtained without a prescription.
No interactions between this treatment and other medicines have been observed to date. However, it should not be mixed with any other products and/or medicinal products.

Pregnancy and breast-feeding
- If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. This product should only be used during pregnancy and breast-feeding on the advice of your doctor.
- If you discover that you are pregnant during treatment, consult with your doctor as only he/she can determine whether you need to continue the treatment.

Driving and using machines
This medicine has no influence on the ability to drive and use machines.

FibCLOT contains up to 3 mmol (or 69 mg) of sodium per vial.
This should be taken into consideration if you are on a low salt diet.

3. HOW TO USE FIBCLOT

Treatment should be initiated under the supervision of a physician experienced in the treatment of congenital fibrinogen deficiency.

Dose
The appropriate dose and frequency will be determined by your doctor and will depend on the following:
- your body weight,
- the severity of your disorder,
- the location and extent of bleeding, or the nature of your surgery,
- your health condition,

Your doctor will recommend that you undergo blood tests during treatment to control your fibrinogen level.
Based on the results of these tests, your doctor may decide to adapt the dose and frequency of your injections.

Frequency of administration
Your doctor will determine how often injections must be administered.
Your doctor will adapt the number of injections based on the severity of your bleeding and the efficacy of the treatment.

Information on frequency and duration of treatment for various situations is shown at the end of this leaflet in the section reserved for health professionals.

Method of administration:
This medicine should be injected into the veins. If you have further questions on use of this product, ask your doctor, pharmacist or nurse.

If you use more FibCLOT than you should
To avoid risk of overdose, your doctor will perform regular blood tests to control your fibrinogen level.
In case of overdose, a risk of abnormal formation of clots in the blood cannot be excluded.

4. POSSIBLE SIDE EFFECTS

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

Risk of allergic reactions: as with any intravenous protein product, allergic reactions may occur. In some cases, these reactions have progressed to a serious allergic reaction.
The warning signs of allergic reactions are:
- swelling of the face or throat,
- feeling of burning and tingling at the injection site,
- chills,
- redness, itching and rash,
- fast heart rate, low blood pressure,
- extreme tiredness (lethargy),
- feeling sick (nausea), vomiting,
- restlessness,
- tightness of the chest,
- pins and needles,
- wheezing (asthma-like).

If one of these effects occurs, **contact immediately a doctor** who will, depending on the type and severity of the reaction, **stop this medicine and/or** start an appropriate treatment.

Blood clots: formation of blood clots may occur in the blood circulation. It may result in:
- heart attack, the warning signs are sudden chest pain or shortness of breath.
- stroke, the warning signs are sudden onset of muscle weakness, loss of sensation and/or balance, decreased alertness or difficulty in speaking.
- a serious condition called pulmonary embolism, the warning signs are chest pain, difficulty in breathing or coughing up blood.
- clot in a vein (venous thrombosis), the warning signs are redness, feel warmth, pain, tenderness, or have a swelling of one or both legs.

If one of these effects occurs, **contact immediately a doctor** who will, depending on the type and severity of the reaction, **stop the treatment with this medicine and/or** start an appropriate treatment.

The following side effects are **common** (may affect up to 1 in 10 infusions):
- headache.

The following side effects are **uncommon** (may affect up to 1 in 100 infusions):
- allergic reaction (including anaphylactic shock, pallor, being sick (vomiting), cough, low blood pressure, chills, hives (urticaria), see also the section "Risk of allergic reactions"),
- dizziness,
- vomiting (associated to headache)
- ringing of the ears,
- blood circulatory disorder (deep vein thrombosis, thrombophlebitis superficial),
- breathing difficulties (asthma),
- skin rash, skin redness, skin irritation, night sweat,
- feeling hot.

Children and adolescents
Frequency, type and severity of side effects are similar in adult and paediatric patients (from birth to less than 18 years of age) except for allergic/anaphylactic type reactions that occurred commonly in paediatric population.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE FIBCLOT

- 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 vial in the outer carton in order to protect from light and moisture.
- The product should be used immediately after reconstitution.
- Do not use this medicine if the reconstituted solution is cloudy or if it has deposits.
- 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 FibCLOT contains
The active substance is human fibrinogen (1.5 g per vial). After reconstitution with 100 mL of water for injections FibCLOT contains 15 mg/mL of human fibrinogen.
The other ingredients are arginine hydrochloride, isoleucine, lysine hydrochloride, glycine, sodium citrate dihydrate and the solvent (water for injections).

What FibCLOT looks like and contents of the pack
This medicine is presented as a powder accompanied by solvent for solution for injections in glass vials and a transfer system.
The reconstituted solution should be almost colourless, slightly opalescent (having a pearl-like shine).

Marketing Authorisation Holder:
Laboratoire français du Fractionnement et des Biotechnologies
Tour W – 102 Terrasse Boieldieu 19ème Étage, 92800 Puteaux, FRANCE
Tel : +33(0) 1 69 82 70 10
Fax : +33(0) 1 69 82 19 03

Manufacturer:
LFB BIOMEDICAMENTS
59 rue de Trévise, 59000 Lille, FRANCE

This medicinal product is authorised in the Member States of the EEA under the following names:
Austria, Germany, Greece, Spain and United Kingdom: FibCLOT
Denmark, Finland, Hungary, Luxembourg, Norway, Sweden, The Netherlands: Fibclot
Belgium: Fibclot 1,5 g, poudre et solvant pour solution injectable/pour perfusion

Italy: Fibriclotte

This leaflet was last revised in 01/2023 .

The following information is intended for healthcare professionals only:

Treatment should be initiated under the supervision of a physician experienced in the treatment of coagulation disorders.

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.

Normal plasma fibrinogen level is in the range of 1.5 - 4.5 g/L. In congenital hypo- or afibrinogenaemia, the critical plasma fibrinogen level below which haemorrhages may occur is approximately 0.5 – 1.0 g/L.

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

Treatment of bleeding and perioperative prophylaxis in patients with congenital hypo- or afibrinogenaemia and known bleeding tendency.

To treat nonsurgical bleeding episodes, it is recommended to raise fibrinogen levels to 1 g/L and maintain fibrinogen at this level until haemostasis is controlled and above 0.5 g/L until healing is complete.
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 controlled and above 0.5 g/L until wound healing is complete.

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

Dose (g) = [target level (g/L) – baseline level (g/L)] x 1/recovery (g/L)/(g/kg) x body weight (kg)

The ratio '1/recovery' is defined from patient's recovery* (see section 5.2), or if recovery is unknown:

- 0.053 (g/kg)/(g/L) for children and adolescents <40 kg body weight
- 0.043 (g/kg)/(g/L) for adults and adolescents ≥40kg body weight.

* Example for patient's recovery and dosing calculation
For a 60 kg patient with undetectable baseline fibrinogen level and fibrinogen increase to 1.20 g/L 1 hour after infusion of 0.060 g per kg of FibCLOT:

- Patient's recovery calculation:
  1.20 (g/L) / 0.060 (g/kg) = 20.0 (g/L)/(g/kg)

– Dose calculation for an increase to 1.0 g/L:
  1.0 g/L x 1 / 20.0 (g/L)/(g/kg) *[or 0.050 (g/kg)/(g/L)]* x 60 kg = 3 g

In case of an emergency situation when the baseline fibrinogen level is not known, the recommended initial dose is 0.05 g per kg of body weight administered intravenously in adults and adolescents ≥40 kg body weight, and 0.06 g/kg of body weight in paediatric patients <40 kg body weight.

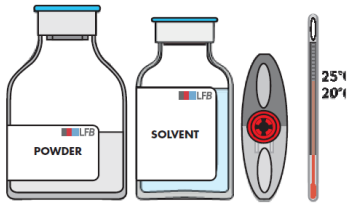
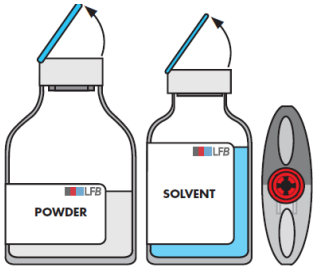
Subsequent posology (doses and frequency of injections) should be adapted based on the patient's clinical status and laboratory results.

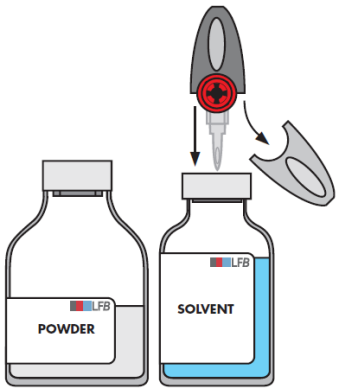
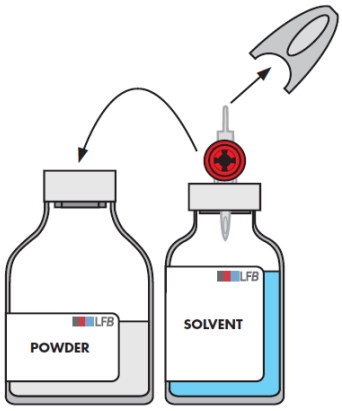
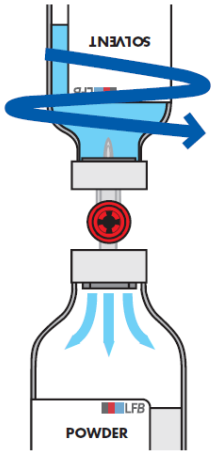
Biological half-life of fibrinogen is 3 - 4 days. Thus, in the absence of consumption, repeated treatment with human fibrinogen is not usually required. Given the accumulation that occurs in case of repeated administration for a prophylactic use, the dose and the frequency should be determined according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

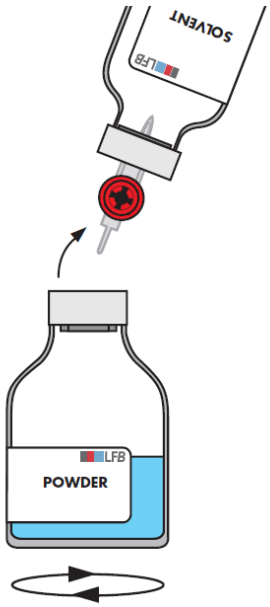
Paediatric population

The recovery and half-life in children and adolescents <40 kg body weight is lower than the one in adults and adolescents ≥40 kg body weight (See section 5.2 of SmPC). Therefore, adapted recoveries should be used to calculate the FibCLOT dose in the respective body weight groups when the individual patient's recovery is unknown. It can be expected that a body weight of <40 kg covers age range from birth up to about 12 years old. The posology (doses and frequency of injections) should be adapted based on the individual clinical response.

Reconstitution:
Use current guidelines for aseptic procedure.

	If necessary, increase the temperature of the two vials (powder and solvent) to ambient temperature.
	Remove the protective cap from the solvent vial and from the powder vial. Disinfect the surface of each stopper.

	Remove the translucent protective sheath from the transfer system and completely insert the exposed piercing spike through the centre of the stopper of the solvent vial while simultaneously twisting the piercing spike.
	Remove the second grey protective sheath from the other end of the transfer system. Turn the solvent vial and quickly push the free end of the piercing spike into the center of the stopper of the powder vial to allow the solvent to transfer into the powder. Ensure that the spike always remains immersed in the solvent to avoid releasing the vacuum prematurely.
	During transfer, direct the jet of solvent over the entire surface of the powder and along the wall of the vial by a rotational horizontal movement. Ensure that all of the solvent is transferred. The vacuum is automatically released at the end of the transfer procedure by sterile air through the venting part of the transfer system.

	Remove the empty vial (solvent) with the transfer system. Gently swirl for a few minutes with a rotating movement to avoid the formation of foam until the powder has completely dissolved.

The reconstituted product should be examined visually prior to administration in order to ensure that it does not contain particulate matter. The reconstituted solution should be almost colourless, slightly opalescent. Do not use solutions which are cloudy or contain deposits.

Administration:
FibCLOT should only be administered intravenously, as a single dose, immediately after reconstitution, at no more than 4 mL/min.

It is recommended to use an infusion set with a 15 µm filter.

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

This medicinal product must not be mixed with other medicinal products and should be administered by a separate injection/infusion line.