PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

FIBRYGA®

Fibrinogen Concentrate (Human)
Powder for Solution for Injection / Infusion, 1 g/vial
ATC-Code: B02BB01

Manufactured by:
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Manufactured for:
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FIBRYGA®

Fibrinogen Concentrate (Human)

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Intravenous use	Powder for solution for injection / infusion 1 g/vial	Glycine, L-Arginine hydrochloride, Sodium chloride, Sodium citrate dihydrate *For a complete listing see section* DOSAGE FORMS, COMPOSITION AND PACKAGING.

DESCRIPTION

FIBRYGA (Fibrinogen Concentrate (Human), 1 g/vial) is a sterile, freeze dried preparation of highly purified fibrinogen.

FIBRYGA is prepared from large pools of human plasma employing precipitations, filtrations and chromatographic steps. Pathogen inactivation/removal is accomplished by a solvent detergent (S/D) method and nanofiltration (20 nm).

INDICATIONS AND CLINICAL USE

FIBRYGA is indicated for the treatment of acute bleeding episodes and perioperative prophylaxis in adult and pediatric patients with congenital afibrinogenemia and hypofibrinogenemia.

Geriatrics (> 65 years of age):

Clinical studies of FIBRYGA did not include subjects age 65 and over to provide evidence as to whether or not they respond differently than younger subjects.

Pediatrics (<18 years of age):

FIBRYGA studies have included eight children (12-17 years). (See Part II, CLINICAL TRIALS)

No data are available in patients below 12 years of age.

CONTRAINDICATIONS

FIBRYGA is contraindicated in individuals who have manifested severe immediate hypersensitivity reactions, including anaphylaxis to FIBRYGA or its components.

WARNINGS AND PRECAUTIONS

General

Products made from human plasma may contain infectious agents, such as viruses and theoretically, the variant Creutzfeldt-Jakob disease (vCJD) agent that can cause disease. The risk that such products will transmit an infectious agent has been reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain current virus infections, and by inactivating and/or removing certain viruses. Despite these measures, such products can still potentially transmit disease. There is also the possibility that unknown infectious agents may be present in such products. Individuals who receive infusions of blood or plasma products may develop signs and/or symptoms of some viral infections.

Allergic Reactions

Allergic reactions may occur. If symptoms of allergic or early signs of hypersensitivity reactions (including hives, generalized urticaria, tightness of the chest, wheezing, hypotension, and anaphylaxis) occur, immediately discontinue administration. The treatment required depends on the nature and severity of the reaction.

Thrombosis

Thrombosis may occur spontaneously in patients with congenital fibrinogen deficiency with or without the use of fibrinogen replacement therapy. Weigh the benefits of FIBRYGA administration versus the risk of thrombosis. Patients receiving FIBRYGA should be monitored for signs and symptoms of thrombosis.

Special Populations

Pregnant Women: The safety of FIBRYGA for use in human pregnancy has not been established in controlled clinical trials. Animal studies have not been conducted to assess the safety with respect to reproduction, development of the embryo or foetus, the course of gestation and peri- and postnatal development. The benefits and risks of administrating FIBRYGA to pregnant women should be carefully weighed.

Nursing Women: The safety of FIBRYGA for use during lactation has not been established in controlled clinical trials and therefore should only be given with caution to breast-feeding mothers.

Monitoring and Laboratory Tests

Determination of the patient's fibrinogen level using an appropriate method, e.g., Clauss fibrinogen assay, is recommended before and during the treatment with FIBRYGA in order to avoid overdosing or underdosing.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

No serious adverse reactions have been reported in clinical studies with FIBRYGA so far. The most serious adverse reactions that may potentially be observed for FIBRYGA are thromboembolic episodes and anaphylactic type reactions.

Clinical Trial Adverse Drug Reactions

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to the rate in the clinical trials of another drug and may not reflect the rates observed in practice.

The clinical safety of FIBRYGA was assessed in two studies in 35 patients with congenital afibrinogenemia, of whom eight were aged 12 to 18 years (see Part II, CLINICAL TRIALS). The majority of the adverse events (AEs) were single instances, such as vomiting, pyrexia, diarrhea, headache, nasopharyngitis and other respiratory tract infections and muscle pain.

Three mild AEs were deemed possibly related to FIBRYGA. These were a case of mild pyrexia and two cases of mild skin reactions, all of which resolved. Four serious adverse events were reported in two patients, and considered related to the underlying disease (abdominal pain and vaginal hemorrhage) or trauma and not related to the study drug.

Post-Market Adverse Drug Reactions

Information on post-market adverse drug reactions is not available for FIBRYGA. The following adverse reactions have been identified during post-approval use of other fibrinogen concentrate products. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or to establish a causal relationship to fibrinogen products:

- Allergic/ anaphylactic reactions: anaphylaxis, dyspnea, rash, tachypnea, hypotension, shock and tachycardia
- Cardiovascular: thromboembolism, pulmonary embolism
- General: chills, fever, nausea, vomiting

DRUG INTERACTIONS

Overview

No interactions of human fibrinogen with other medicinal products or concurrent illnesses are known.

Drug-Drug Interactions

FIBRYGA should not be mixed with other medicinal products.

Drug-Food Interactions

Interactions with food have not been established.

Drug-Herb Interactions

Interactions with herbal products have not been established.

Drug-Lifestyle Interactions

Effects on ability to drive and use machines have not been established.

DOSAGE AND ADMINISTRATION

Recommended Dose and Dosage Adjustment

FIBRYGA dosing, duration of dosing and frequency of administration should be individualized based on the extent of bleeding, laboratory values, and the clinical condition of the patient.

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.

The recommended target fibrinogen plasma level is 100 mg/dL for minor bleeding or minor surgery and 150 mg/dL for major bleeding or major surgery.

FIBRYGA dose when baseline fibrinogen level is known

Dose should be individually calculated for each patient based on the target plasma fibrinogen level based on the type of bleeding, actual measured plasma fibrinogen level and body weight, using the following formula:

$$\text{Dose (mg/kg body weight)} = \frac{[\text{Target level (mg/dL)} - \text{measured level (mg/dL)}]}{1.8 \text{ (mg/dL per mg/kg body weight)}}$$

FIBRYGA dose when baseline fibrinogen level is not known

If the patient's fibrinogen level is not known, the recommended dose is 60 mg per kg of body weight administered intravenously.

Monitoring of patient's fibrinogen level is recommended during treatment with FIBRYGA.

Administration

For intravenous use only. Prior to use, allow FIBRYGA to reach ambient room temperature.

Do not use solutions that are cloudy or have deposits.

Reconstitution:

Vial Size	Volume of WFI to be Added to Vial	Approximate Available Volume	Nominal Concentration per mL
1g	50 ml	50 ml	20 mg

1. Warm both the powder and water for injection (WFI) in closed bottles up to 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 caps of the bottles. The temperature of the water bath should not exceed +37°C (98°F).
2. Remove the cap from the concentrate (FIBRYGA) bottle and the WFI to expose the central portion of the infusion stopper. Clean the rubber stopper with an alcohol swab and allow the rubber stopper of the bottles to dry.
3. Peel away the lid of the outer package of the Octajet transfer device. To maintain sterility, leave the Octajet device in the clear outer packaging.
4. Take the Octajet in its outer package and invert it over the concentrate (FIBRYGA) bottle. Place device while in the outer package onto the center of the FIBRYGA bottle until the clips of the product spike (colorless) are locked. While holding onto the concentrate bottle, carefully remove the outer package from the Octajet, being careful to not touch the water spike (blue) and leave the Octajet attached firmly to the concentrate bottle. (Fig. 1)

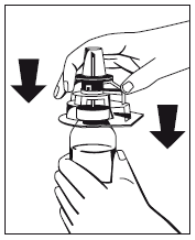

Fig. 1

5. With the concentrate (FIBRYGA) bottle held firmly on a level surface, invert the WFI bottle and place it at the center of the water spike. Push the blue plastic cannula of the Octajet firmly through the rubber stopper of the WFI bottle. (Fig. 2)

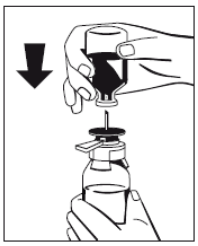

Fig. 2

6. Remove the distance ring (Fig. 3) and press the WFI bottle down (Fig. 4). WFI will flow into the concentrate (FIBRYGA) bottle.

Fig. 3

Fig. 4

7. When transfer of the WFI is complete, gently swirl the product bottle until the powder is fully dissolved. Do not shake the bottle to avoid foam formation. The powder should be dissolved completely within approximately 5 minutes. It should not take longer than 30 minutes to dissolve the powder.
8. Turn the blue WFI bottle connector (both directions possible) to bring position markers together and remove WFI bottle together with the water spike. (Fig. 5)

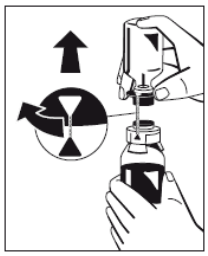

Fig. 5

9. Place the provided filter on the remaining Luer Lock on the concentrate bottle (Fig. 6) and withdraw the solution through the filter into the syringe. (Fig. 7,8)

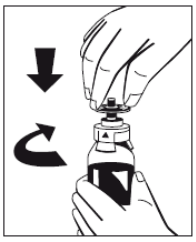

Fig. 6

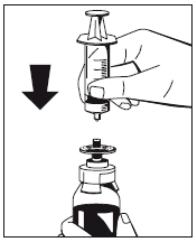

Fig. 7

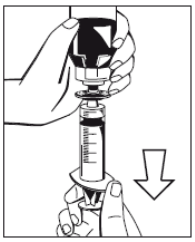

Fig. 8

10. Detach the filled syringe from the filter and discard the empty bottle.

FIBRYGA should be administered slowly intravenously at a recommended maximum rate of 5 ml per minute.

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

Precautions

FIBRYGA should not be mixed with other medicinal products. A separate intravenous line should be used for injection. Do not use the product after expiry date.

OVERDOSAGE

No cases of overdose have been reported.

For management of a suspected drug overdose, contact your regional Poison Control Centre.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Fibrinogen (factor I) is a soluble plasma protein that, during the coagulation process, is converted to fibrin, one of the key components of the blood clot. Fibrinogen is a heterohexamer with a molecular weight of 340 kDa and composed of two sets of A*alpha*, B*beta*, and *gamma* polypeptide chains.

Following coagulation activation and thrombin generation, fibrinogen is cleaved by thrombin at specific sites on A*alpha* and B*beta* chains to remove fibrinopeptide A (FPA) and fibrinopeptide B (FPB). The removal of FPA and FPB exposes binding sites on fibrinogen and leads to the formation of fibrin monomers that subsequently undergo fibrin polymerization. The resulting fibrin is stabilized in the presence of calcium ions and by activated factor XIII. Factor XIIIa acts on fibrin to form cross links between fibrin polymers and renders the fibrin clot more resistant to fibrinolysis. The end product of the coagulation cascade is cross-linked fibrin which stabilizes the primary platelet plug and achieves secondary hemostasis.

Pharmacodynamics

Administration of FIBRYGA provides an increase in plasma fibrinogen level and can temporarily correct the coagulation defect of patients with congenital fibrinogen deficiency.

Pharmacokinetics

An open label, prospective, randomized, controlled, two-arm cross-over study was conducted in 22 patients with congenital fibrinogen deficiency (afibrinogenemia), ranging in age from 12 to 53 years (6 adolescents, 16 adults). In this cross-over study, these results were compared to the same parameters of another fibrinogen concentrate (RiaSTAP™) available in Canada in the same subjects. Each subject received a single intravenous 70 mg/kg dose of FIBRYGA and the comparator product. Blood samples were drawn from the patients to determine the fibrinogen activity at baseline and up to 14 days after the infusion. The pharmacokinetic parameters are summarized in Table 1. The mean values for the AUCnorm (primary endpoint) for fibrinogen activity following administration of FIBRYGA were significantly higher than after administration of RiaSTAP™.

No statistically relevant difference was observed between males and females for fibrinogen activity. In the per-protocol analysis, subjects less than 18 years of age (n=5) had small differences including a shorter half life than in adults. The number of subjects less than 18 years of age in this study limits statistical interpretations.

The incremental in vivo recovery (IVR) was determined from plasma levels obtained up to 4 hours post-infusion. The mean incremental IVR for FIBRYGA was 1.8 mg/dL increase per mg/kg. The mean in vivo recovery indicates that a dose of 70 mg/kg will increase patients'

fibrinogen plasma concentration by approximately 125 mg/dL.

Table 1: Pharmacokinetic Parameters (n=21) for Fibrinogen Activity

Parameters	**FIBRYGA Activity Mean ± SD (range)**	**RiaSTAP™ Activity Mean ± SD (range)**	% Ratio of Geometric Means*	90% Confidence Interval Mean Ratio*†
Half-life [hr]	75.9± 23.8 (40.0-157.0)	69.4 ± 16.0 (48.6–101.9)	108.0	95.4, 122.4
C_{max} [mg/dL]	139.0 ± 36.9 (83.0-216.0)	126.5 ± 30.9 (85.0–199.0)	109.1	102.3, 116.2
AUC_{norm}	1.62 ± 0.45 (0.85–2.51)	1.38 ± 0.47 (0.76–2.46)	119.6	111.7, 128.1
Clearance [mL/hr/kg]	0.67 ± 0.20 (0.40-1.17)	0.80 ± 0.26 (0.41–1.31)	83.6	78.1, 89.5
Mean residence time [hr]	106.3 ± 30.9 (58.7-205.5)	99.0± 20.8 (72.4–141.2)	106.1	94.4, 119.2
Volume of distribution at steady state [mL/kg]	70.2 ± 29.9 (36.9-149.1)	76.6 ± 19.6 (47.9–113.7)	88.6	79.1, 99.4

*Geometric mean derived from the ANOVA model on log transformed values. †Not adjusted for multiplicity.
C_{max} = maximum plasma concentration; AUC_{norm} = area under the curve normalised to the dose administered;
SD = standard deviation

Absorption: Since FIBRYGA is administered intravenously, the product is available immediately. Bioavailability is proportional to the dose administered.

STORAGE AND STABILITY

FIBRYGA can be stored at +2 °C to +25 °C for up to 36 months from the date of manufacture. Do not use product after expiry date.

FIBRYGA contains no preservatives. Stability of the reconstituted solution has been demonstrated for up to 24 hours at + 25°C. From a microbiologic point of view, unless the method of opening/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. Discard partially used bottles.

Do not freeze. Protect from exposure to light. Keep in a safe place out of the reach and sight of children.

SPECIAL HANDLING INSTRUCTIONS

FIBRYGA should be inspected visually for particulate matter and discolouration prior to administration. Do not use non-homogenous solutions, or those that have a deposit. Any remaining fraction should be discarded. FIBRYGA should be warmed up to room or body temperature before use.

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

DOSAGE FORMS, COMPOSITION AND PACKAGING

FIBRYGA is supplied in a single-use bottle containing the labeled amount of functionally active fibrinogen. The components used in the packaging for FIBRYGA are latex-free. FIBRYGA is a powder for solution for intravenous injection/ infusion.

The following dosage forms are available: 1g

Nature and Contents of Container

Each vial of reconstituted FIBRYGA contains 1 g of the active ingredient human fibrinogen. Each package contains 1 glass bottle of FIBRYGA, a transfer device (Octajet), a particle filter and the package leaflet.

Composition:

Human Fibrinogen	1 g
Sodium chloride	300 mg
Sodium citrate dihydrate	75 mg
Glycine	500 mg
L-Arginine hydrochloride	500 mg

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: FIBRYGA®

Chemical name: Human Fibrinogen

Molecular formula and molecular mass: 340 kD

Structural formula: not applicable

Physicochemical properties: Fibrinogen is a soluble plasma glycoprotein of about 340 kD. The protein is a heterohexamer, composed of three pairs of polypeptides, namely two Aα–, two Bβ– and two γ–chains.

Product Characteristics

FIBRYGA (Fibrinogen (Human), 1 g/vial) is a sterile freeze dried preparation of highly purified fibrinogen derived from human plasma. It is prepared from large pools of human plasma employing precipitations, filtrations and chromatographic steps. Pathogen inactivation/removal is accomplished by a solvent detergent (S/D) method and a nanofiltration (20 nm).

Pathogen Safety

The pathogen safety of FIBRYGA is ensured through dedicated steps, in particular by the solvent/detergent treatment which inactivates enveloped viruses such as HIV, hepatitis B (HBV) and hepatitis C (HCV) virus and by nanofiltration (20 nm) for removal of both enveloped viruses and non-enveloped viruses such as hepatitis A virus (HAV) and parvovirus B19. Furthermore, the nanofiltration also removes potentially present infectious prion protein of an experimental agent of transmissible spongiform encephalopathy (TSE), considered a prudent model for Creutzfeldt-Jakob disease (CJD) and its variant form (vCJD).

CLINICAL TRIALS

Pharmacokinetic and functional activity study

An open label, prospective, randomized, controlled, two-arm cross-over study was conducted in 22 patients with congenital fibrinogen deficiency (afibrinogenemia), ranging in age from 12 to 53 years (6 adolescents, 16 adults). In this cross-over study, these results were compared to the same parameters of another Fibrinogen concentrate (RiaSTAP™) available in Canada in the same subjects. Each subject received a single intravenous 70 mg/kg dose of FIBRYGA and the

comparator product. Blood samples were drawn from the patients to determine the fibrinogen activity at baseline and up to 14 days after the infusion.

The pharmacokinetic study evaluated the single-dose PK (see Part I, Action and Clinical Pharmacology, pharmacokinetics) and maximum clot firmness (MCF) in subjects with afibrinogenemia. MCF was determined by thromboelastometry (ROTEM®) testing and measured to demonstrate functional activity of replacement fibrinogen.

For each subject, the MCF was determined before (baseline) and one hour after the single dose administration of FIBRYGA or RiaSTAP™. The mean changes from pre-infusion to 1 hour post-infusion were 9.68 mm (95% CI: 8.37, 10.99) and 10.00 mm (95% CI: 8.07, 11.93), after administration of FIBRYGA or RiaSTAP™, respectively.

Safety and Efficacy study

A planned interim analysis of an ongoing prospective, open label, uncontrolled, multicentre phase III study was conducted in 13 patients with congenital fibrinogen deficiency (afibrinogenemia), ranging in age from 13 to 53 years (2 adolescents, 11 adults). Eleven patients were treated on-demand for 23 bleeding episodes and 4 patients underwent 4 surgical procedures. Of the 23 bleeding events (BEs), 16 (69.6%) were spontaneous and 7 (30.4%) were traumatic and all these BEs were minor.

For the treatment of the first bleeding episode, the patients received a median dose of FIBRYGA of 58.8 mg/kg (mean ± standard deviation [SD] 53.7 ± 14.3; range 33.9–71.4 mg/kg) per infusion. The median number of infusions for BEs was 1. Two (8.7%) BEs required 2 infusions (these were the first BEs in 2 patients). No BEs required more than 2 infusions. The median dose of FIBRYGA per infusion for treatment of all 23 BEs was 57.5 mg/kg.

All the treated bleeding episodes and surgical procedures were rated as successful (rating of good or excellent efficacy) by an independent adjudication committee using an objective scoring system.

The efficacy of FIBRYGA for surgical prophylaxis was assessed in 4 surgical procedures in 4 patients; 3 procedures were classified as minor and 1 was classified as major (eye enucleation with socket reconstruction). Median (range) loading FIBRYGA dose administered for all surgeries was 70 mg/kg (65.79-102.56 mg/kg). One minor surgery required 2 and the major surgery required 7 additional post-operative infusions as per fibrinogen activity recommendations in the protocol. Median (range) FIBRYGA dose administered post-operatively was 20.50 mg/kg (12.82-34.09 mg/kg). The overall success rate (rate of good or excellent efficacy) was 100% as assessed by the independent adjudication committee using an objective scoring system.

MCF was determined before (baseline) and one hour after the first FIBRYGA infusion for the first 11 bleeding episodes for each of the 11 patients. The observed mean change in MCF from baseline to 1 hour after the first infusion of FIBRYGA was 6.4 mm (95% CI: 4.55, 8.17).

There were no reports of related serious adverse events, deaths, thromboembolism and severe allergic or hypersensitivity reactions. Two patients had inhibitors to fibrinogen at baseline (pre-existing antifibrinogen antibodies), and no patients developed the new inhibitor during studies..

TOXICOLOGY

Single Dose Toxicity

Two GLP-compliant single dose toxicity studies were performed with FIBRYGA in doses of up to 500 mg/ kg b.w. in rats and up to 1000 mg/ kg b.w. in mice. In both studies no mortality, no test item-related clinical signs and no macroscopic findings were observed.

Repeated Dose Toxicity

Repeated dose toxicity testing in animals with human protein preparations is impracticable due to the induction of, and the interference with antibodies. Therefore no studies were conducted with FIBRYGA.

Reproductive Toxicity

No studies were conducted with FIBRYGA.

Local Tolerance

The local tolerance of FIBRYGA was tested in two studies after intravenous and intra-arterial and paravenous administration to rabbits. The animals were observed for 96 hours and then sacrificed for histological evaluation of the injection sites.
FIBRYGA was well tolerated, no general or relevant local changes, and no histological noticeable findings were observed.

Mutagenicity and Carcinogenicity

No studies were conducted with FIBRYGA.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

FIBRYGA®
Fibrinogen Concentrate (Human)

Read this carefully before you start taking FIBRYGA and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about FIBRYGA.

What is FIBRYGA used for?

FIBRYGA is used for the treatment of acute bleeding episodes and perioperative prophylaxis in children and adults with congenital afibrinogenemia and hypofibrinogenemia.

How does FIBRYGA work?

FIBRYGA is a human fibrinogen presented as a powder for solution for intravenous administration (i.e. infusion into a vein). Fibrinogen is a normal constituent of the human blood and supports the blood coagulation of your body. Adequate doses of FIBRYGA may restore abnormally low fibrinogen levels to levels necessary for controlling bleeding.

What are the ingredients in FIBRYGA?

Medicinal ingredients: Fibrinogen (Human)
Non-medicinal ingredients: Sodium chloride, Sodium citrate dihydrate, Glycine, L-Arginine hydrochloride

FIBRYGA comes in the following dosage forms:

FIBRYGA is a powder for solution for intravenous injection and comes in the following dosage forms: 1g

Do not use FIBRYGA if:

- you are allergic to human fibrinogen or any of the other ingredients contained in FIBRYGA.
- you have experienced allergic reactions to FIBRYGA in the past.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take FIBRYGA. Talk about any health conditions or problems you may have, including:

- Allergic reactions (e.g. reddening of the skin, skin rash, itching, fall in blood pressure, difficulty in breathing)
- General symptoms (e.g. chills, fever, nausea, vomiting)

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with FIBRYGA:

FIBRYGA should not be mixed with other products.

How to take FIBRYGA:

FIBRYGA is injected into a vein. The product should not be used if it looks cloudy or is leaking. It should be warmed up to room or body temperature before use. Discard any remaining contents after use. Do not use the product after its expiry date (printed on the bottle).

Usual dose:

Your doctor will determine the dose(s) of FIBRYGA. The dose and dosage regimen is dependent on the indication and may need to be individualised for each patient. Doses may be adjusted over time to achieve the desired clinical response and plasma fibrinogen levels.

Overdose:

No cases of overdose with human fibrinogen products have been reported.

If you think you have taken too much FIBRYGA, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

What are possible side effects from using FIBRYGA?

- The following side effects have been observed in studies with FIBRYGA: a case of mild pyrexia and two cases of mild skin reactions.

The following side effects have been observed for other fibrinogen products and may potentially also occur after FIBRYGA administration:

- Allergic/ anaphylactic reactions: anaphylaxis, dyspnea, rash, tachypnea, hypotension, shock and tachycardia
- Cardiovascular: thromboembolism, pulmonary embolism
- General: chills, fever, nausea, vomiting

If any of the above listed symptoms occur, are severe or if they worry you, talk to your doctor or pharmacist. These are not all the possible side effects you may feel when taking FIBRYGA. For any unexpected effects while taking FIBRYGA, contact your doctor or pharmacist.
If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects
You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.
3 ways to report:

- Online at MedEffect;
- By calling 1-866-234-2345 (toll-free);
- By completing a Patient Side Effect Reporting Form and sending it by:
  - Fax to 1-866-678-6789 (toll-free), or
  - Mail to: Canada Vigilance Program
    Health Canada, Postal Locator 0701E
    Ottawa, ON
    K1A 0K9

    Postage paid labels and the Patient Side Effect Reporting Form are available at MedEffect.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:
Store at +2 °C to +25°C for up to 36 months.
Do not freeze. Protect from light. Discard any remaining contents after use. Do not use after expiry date.

Keep out of reach and sight of children.

If you want more information about FIBRYGA:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website; the manufacturer's website http://www.octapharma.ca, or by calling 1-888-438-0488.

This leaflet was prepared by Octapharma Pharmazeutika Produktionsges.m.b.H

Last Revised <March-21-2018>