HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use FIBRYNA safely and effectively. See full prescribing information for FIBRYNA.

FIBRYNA®, Fibrinogen (Human)
Lyophilized Powder for Reconstitution, For Intravenous Use
Initial U.S. Approval: YYYY

--------------------INDICATIONS AND USAGE---------------------
FIBRYNA is a human fibrinogen concentrate indicated for the treatment of acute bleeding episodes in adults and adolescents with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia (1).
FIBRYNA is not indicated for dysfibrinogenemia.

---------------------DOSEAGE AND ADMINISTRATION-----------------
For intravenous use only (1). Reconstitute prior to use.
• Dose when fibrinogen level is known (2.1):
Dose (mg/kg body weight) =
(Target fibrinogen level (mg/dL) - measured fibrinogen level (mg/dL)) \div 1.8 (mg/dL per mg/kg body weight)
The recommended target fibrinogen plasma level is 100 mg/dL for minor bleeding and 150 mg/dL for major bleeding.
• Dose when fibrinogen level is unknown: 70 mg/kg body weight (2.1).
• The injection rate should not exceed 5 mL per minute (2.3).
• Monitoring of patient’s fibrinogen level is recommended during treatment.

--------------------DOSEAGE FORMS AND STRENGTHS-----------------
FIBRYNA is available as a lyophilized powder in single-use bottles containing approximately 1 g fibrinogen concentrate per bottle (3).

-------------------CONTRAINDICATIONS-----------------------------
Anaphylactic or severe reactions to FIBRYNA or its components (4).

-------------------WARNINGS AND PRECAUTIONS----------------------
• Monitor patients for early signs of hypersensitivity or allergic reactions. If necessary, discontinue administration and institute appropriate treatment (5.1).
• Thrombotic events have been reported in patients receiving human fibrinogen concentrate. Treatment with human fibrinogen concentrate has been associated with thrombosis at target plasma fibrinogen levels that were below 150mg/dL. The thrombotic risks may be greater when the target fibrinogen plasma level is 150mg/dL. Weigh the benefits of administration versus the risks of thrombosis (5.2).
• FIBRYNA is made from pooled human plasma. Products made from human plasma may contain infectious agents, e.g., viruses and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent (5.3).

-------------------ADVERSE REACTIONS-----------------------------
The most serious adverse reactions that may be observed for FIBRYNA are thromboembolic episodes and anaphylactic type reactions. The most common adverse reactions observed in more than one subject in clinical studies with FIBRYNA (> 5% of subjects) were vomiting, weakness and pyrexia (fever) (6).

To report SUSPECTED ADVERSE REACTIONS, contact Octapharma at 1-866-766-4860 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

-------------------USE IN SPECIFIC POPULATIONS---------------------
• Pediatric: There was no difference in the pharmacokinetics of FIBRYNA between adults and adolescents (12-17 years of age) (8.4).

See 17 for PATIENT COUNSELING INFORMATION.

Revised: [MM/YYYY]
1 INDICATIONS AND USAGE
FIBRYNA is a human fibrinogen concentrate indicated for the treatment of acute bleeding episodes in adults and adolescents with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia.

FIBRYNA is not indicated for dysfibrinogenemia.

2 DOSAGE AND ADMINISTRATION
For intravenous use after reconstitution. Reconstitute prior to use.

2.1 Dosage
FIBRYNA 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 recommended target fibrinogen plasma level is 100 mg/dL for minor bleeding and 150 mg/dL for major bleeding.

FIBRYNA dose when baseline fibrinogen level is known
Dose should be individually calculated for each patient based on the target plasma fibrinogen level for the type of bleeding, actual measured plasma fibrinogen level and body weight, using the following formula (see Pharmacokinetics [12.3]):

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

FIBRYNA dose when baseline fibrinogen level is not known
If the patient’s fibrinogen level is not known, the recommended dose is 70 mg per kg of body weight administered intravenously.

Monitor the patient’s fibrinogen level during treatment with FIBRYNA.
Additional infusions of FIBRYNA should be administered if the plasma fibrinogen level is below the accepted lower limit (80 mg/dL for minor bleeding, 130 mg/dL for major bleeding) of the target level until hemostasis is achieved.

2.2 Preparation and Handling
FIBRYNA package contains:
- 1 single-use bottle of FIBRYNA concentrate
- 1 transfer device (Octajet)
- 1 particle filter

Reconstitute FIBRYNA with 50 mL of sterile Water for Injection (not provided).
Do not use FIBRYNA beyond the expiration date. FIBRYNA contains no preservatives. Use aseptic technique when preparing and reconstituting FIBRYNA.

The procedures below are provided as general guidelines for preparation and reconstitution of FIBRYNA.

Reconstitute FIBRYNA as follows:
1. Warm both the powder and sterile Water for Injection(sWFI) in their closed bottles to room temperature. This temperature should be maintained during reconstitution. If a water bath is used for warming, prevent water from 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 FIBRYNA bottle and the sWFI bottle to expose the central portion of the rubber stoppers. Clean the rubber stoppers with an alcohol swab and allow the rubber stoppers 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 package.
4. Take the Octajet in its outer package and invert it over the FIBRYNA bottle. Place the device while in the outer package onto the center of the FIBRYNA bottle until the clips of the product spike (colorless) are locked. While holding onto the FIBRYNA bottle, carefully remove the outer package from the Octajet, being careful not to touch the water spike (blue) and leave the Octajet attached firmly to the FIBRYNA bottle. (Fig. 1)

5. With the FIBRYNA bottle held firmly on a level surface, invert the sWFI 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 sWFI bottle. (Fig. 2)

6. Remove the distance ring (Fig. 3) and press the sWFI bottle down (Fig. 4). sWFI will flow into the FIBRYNA bottle.

7. When transfer of the sWFI is complete, gently swirl the FIBRYNA bottle until the powder is fully dissolved. To avoid foam formation, do not shake the bottle. The powder should be dissolved completely within approximately 5 to 10 minutes.

8. Turn the blue sWFI bottle connector (both directions possible) to bring the position markers together and remove the sWFI bottle together with the water spike (Fig. 5). Keep the concentrate bottle upright to avoid leaking.

9. Firmly connect the provided particle filter on the remaining Luer Lock on the FIBRYNA bottle (Fig. 6) and withdraw the solution through the particle filter into the syringe. (Fig. 7,8)

10. Detach the filled syringe from the particle filter and discard the empty bottle and the filter.
• After reconstitution, the FIBRYNA solution should be almost colorless and slightly opalescent. Inspect the reconstituted FIBRYNA solution in the syringe for visible particulate matter and discoloration prior to administration. Do not use if particulate matter or discoloration are observed.

The powder should be reconstituted only directly before injection. After reconstitution, do not refrigerate or freeze the FIBRYNA solution. Use the reconstituted FIBRYNA solution immediately or within 4 hours after reconstitution. Discard any remaining FIBRYNA solution.

2.3 Administration
For intravenous use only after reconstitution.
• Do not administer FIBRYNA in the same tubing or container as other medications.
• Use aseptic technique when administering FIBRYNA.
• Administer FIBRYNA at room temperature by slow intravenous injection at a rate not exceeding 5 mL per minute.

3 DOSAGE FORMS AND STRENGTHS
FIBRYNA is a sterile, lyophilized powder for reconstitution for intravenous injection. FIBRYNA is provided in single-use bottles containing approximately 1 g fibrinogen concentrate for reconstitution with 50 mL of sterile Water for Injection.

4 CONTRAINDICATIONS
FIBRYNA is contraindicated in individuals who have manifested severe immediate hypersensitivity reactions, including anaphylaxis, to FIBRYNA or its components (Sodium Citrate Dihydrate; Glycine; L-Arginine hydrochloride).

5 WARNINGS AND PRECAUTIONS
5.1 Hypersensitivity Reactions
Hypersensitivity reactions may occur. If early signs of hypersensitivity reactions (including hives, generalized urticaria, tightness of the chest, wheezing, hypotension, and anaphylaxis) or symptoms of allergic reactions occur, immediately discontinue administration (see Patient Counseling Information). The treatment required depends on the nature and severity of the reaction.

5.2 Thrombosis
Thrombosis may occur spontaneously in patients with congenital fibrinogen deficiency with or without the use of fibrinogen replacement therapy. Thrombotic events have been reported in patients receiving human fibrinogen concentrate. Treatment with human fibrinogen concentrate has been associated with risk of thrombosis at target fibrinogen levels that were less than 150mg/dL. The risk of thrombosis may be greater when the target fibrinogen plasma level is 150mg/dL. Weigh the benefits of FIBRYNA administration versus the risks of thrombosis. Patients receiving FIBRYNA should be monitored for signs and symptoms of thrombosis. (see Patient Counseling Information)

5.3 Transmissible Infectious Agents
FIBRYNA is made from human plasma. Products made from human plasma may contain infectious agents (e.g., viruses and the CJD agent that can cause disease. Also, unknown infectious agents may be present in such products (see Patient Counseling Information). 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 a process demonstrated to inactivate and/or remove certain viruses during manufacturing. (see Description [11]). Despite these measures, such products may transmit disease. All infections thought by a physician possibly to have been transmitted by this product should be reported by the physician or other healthcare provider to Octapharma at 1-866-766-4860.

6 ADVERSE REACTIONS
The most serious adverse reactions that may potentially be observed for FIBRYNA are thromboembolic episodes and anaphylactic type reactions.

6.1 Clinical Trials Experience
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.
Thirteen subjects received at least one dose of FIBRYNA for the treatment of bleeding episodes and/or perioperative management of bleeding. The most common adverse reactions observed in more than one subject in clinical studies with FIBRYNA (> 5% of subjects) were vomiting, weakness and pyrexia (fever).

One patient had a mild skin reaction (itchiness and redness) after FIBRYNA administration for a bleeding episode and was treated with diphenhydramine and hydrocortisone. Thereafter, the patient received another infusion of FIBRYNA for the treatment of the same bleeding episode and another FIBRYNA infusion for surgical prophylaxis during next week. For both of those FIBRYNA infusions the patient was treated with diphenhydramine and hydrocortisone prophylactically and did not experience any drug reactions.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no data with FIBRYNA use in pregnant women to determine whether there is a drug-associated risk. Animal reproduction studies have not been conducted with FIBRYNA. It is not known whether FIBRYNA can cause fetal harm when administered to a pregnant woman or can affect fertility. FIBRYNA should be given to a pregnant woman only if clearly needed. In the U.S. general population, the estimated background risk of major birth defect and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

8.2 Lactation

Risk Summary

There is no information regarding the presence of FIBRYNA in human milk, the effect on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for FIBRYNA and any potential adverse effects on the breastfed infant from FIBRYNA or from the underlying maternal condition.

8.4 Pediatric Use

There was no difference in the pharmacokinetics of FIBRYNA between adults and adolescents (12-17 years of age).

8.5 Geriatric Use

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

11 DESCRIPTION

FIBRYNA is a human plasma-derived, sterile, purified, virus-inactivated and nanofiltered (20 nm) fibrinogen concentrate. FIBRYNA is supplied as a lyophilized powder for reconstitution for intravenous injection. FIBRYNA contains no preservatives. Each bottle contains approximately 1 g of fibrinogen. The diluent for reconstitution of the lyophilized powder is sterile Water for Injection.

The nominal composition of FIBRYNA is as follows:

<table>
<thead>
<tr>
<th>Component</th>
<th>Quantity/ mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human Fibrinogen</td>
<td>20 mg</td>
</tr>
<tr>
<td>Sodium Chloride</td>
<td>6 mg</td>
</tr>
<tr>
<td>Sodium Citrate Dihydrate</td>
<td>1.5 mg</td>
</tr>
<tr>
<td>Glycine</td>
<td>10 mg</td>
</tr>
<tr>
<td>L-Arginine Hydrochloride</td>
<td>10 mg</td>
</tr>
</tbody>
</table>

All units of human plasma used in the manufacture of FIBRYNA are provided by FDA-approved blood establishments, and are tested by FDA-licensed serological tests for Hepatitis B surface antigen (HBsAg), antibodies to Hepatitis C Virus (HCV) and Human Immunodeficiency Virus (HIV)-1/2. As an additional safety measure, the plasma is tested with Nucleic Acid Tests (NATs) for Hepatitis A Virus (HAV), Hepatitis B Virus (HBV), HCV and HIV-1 and found to be non-reactive (negative). The plasma is also screened for Human Parvovirus (B19V) by NAT. The limit for B19V DNA in the mini-pool is set not to exceed $10^3$ IU/mL. Only plasma that passed virus screening is used for production.
The FIBRYNA manufacturing process includes a solvent/detergent (S/D) step for virus inactivation, and a nanofiltration step (Planova 20N nanofilter or Pegasus SV4 nanofilter) for virus removal. The mean cumulative virus reduction factors of these steps are summarized in Table 1 below.

### Table 1: Cumulative Virus Reduction Factors (Log_{10}) During FIBRYNA Manufacture

<table>
<thead>
<tr>
<th>Production Step</th>
<th>Enveloped Viruses</th>
<th>Non-Enveloped Viruses</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HIV-1</td>
<td>PRV</td>
</tr>
<tr>
<td><strong>S/D treatment</strong></td>
<td>≥ 5.2</td>
<td>6.6</td>
</tr>
<tr>
<td><strong>Nanofiltration (Planova 20N)</strong></td>
<td>≥ 4.2</td>
<td>≥ 6.6</td>
</tr>
<tr>
<td><strong>Cumulative Virus Reduction Factor (Log_{10})</strong></td>
<td>≥ 9.4</td>
<td>≥ 13.2</td>
</tr>
</tbody>
</table>

PRV: Pseudorabies Virus, model for large enveloped DNA viruses  
BVDV: Bovine Virus Diarrhea Virus, model for HCV  
PPV: Porcine Parvovirus, model for B19V  
n.a.: not applicable  
* When the nanofiltration step was performed using a Pegasus SV4 nanofilter, the virus reduction factors for HIV-1, PRV, BVDV, HAV, and PPV were ≥ 3.9, ≥ 6.3, ≥ 5.0, ≥ 5.2, and 4.5, respectively. The cumulative virus reduction factors (S/D treatment + Pegasus SV4 nanofiltration) were ≥ 9.0, ≥ 12.9, ≥ 10.8, ≥ 5.2, and 4.5, respectively.

## 12 CLINICAL PHARMACOLOGY

### 12.1 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\textalpha, B\textbeta, and gamma polypeptide chains.

Following coagulation activation and thrombin generation, fibrinogen is cleaved by thrombin at specific sites on the A\textalpha and B\textbeta chains to remove fibrinopeptide A (FPA) and fibrinopeptide B (FPB). The removal of FPA and FPB exposes binding sites on the fibrinogen molecule and leads to the formation of fibrin monomers that subsequently undergo polymerization. The resulting fibrin is stabilized 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.

### 12.2 Pharmacodynamics

Administration of FIBRYNA to patients with congenital fibrinogen deficiency supplements the missing coagulation factor or increases low plasma fibrinogen levels. Normal plasma fibrinogen level is in the range of 200 - 450 mg/dL.

An open-label, prospective, randomized, controlled, two-arm, cross-over study was conducted in 22 subjects with congenital fibrinogen deficiency (afibrinogenemia), ranging in age from 12 to 53 years (6 adolescents, 16 adults). Each subject received a single intravenous 70 mg/kg dose of FIBRYNA and the comparator product. Blood samples were drawn from the patients to measure the fibrinogen activity at baseline and up to 14 days after the infusion.—Maximum Clot Firmness (MCF) was measured by thromboelastometry (ROTEM).

For each subject, MCF was determined before (baseline) and one hour after the single dose administration of FIBRYNA. In this cross-over study, the results were compared with another fibrinogen concentrate available on the US market. The results of the study demonstrated that the MCF values were significantly higher after administration of FIBRYNA than at baseline (see Table 2). The mean change from pre-infusion to 1 hour post-infusion was 9.7 mm in the primary analysis (9. mm for subjects < 18 years old and 9.9 mm for subjects ≥ 18 to < 65 years old).

### Table 2: MCF [mm] (ITT population) n=22

<table>
<thead>
<tr>
<th>Time point</th>
<th>Mean ± SD</th>
<th>Median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-infusion</td>
<td>0 ± 0</td>
<td>0 (0-0)</td>
</tr>
</tbody>
</table>
### Table 3: Pharmacokinetic Parameters (n=21) for Fibrinogen Activity

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean ± SD (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Half-life [hr]</td>
<td>75.9 ± 23.8 (40.0-157.0)</td>
</tr>
<tr>
<td>Cmax [mg/dL]</td>
<td>139.0 ± 36.9 (83.0-216.0)</td>
</tr>
<tr>
<td>AUC [mg*hr/mL]</td>
<td>124.8 ± 34.6 (65.7-193.3)</td>
</tr>
<tr>
<td>AUC\textsuperscript{norm} for dose of 70 mg/kg [mg*hr/mL]</td>
<td>113.7 ± 31.5 (59.7-175.5)</td>
</tr>
<tr>
<td>Clearance [mL/hr/kg]</td>
<td>0.7 ± 0.2 (0.4-1.2)</td>
</tr>
<tr>
<td>Mean residence time [hr]</td>
<td>106.3 ± 30.9 (58.7-205.5)</td>
</tr>
<tr>
<td>Volume of distribution at steady state [mL/kg]</td>
<td>70.2 ± 29.9 (36.9-149.1)</td>
</tr>
</tbody>
</table>

C<sub>max</sub> = maximum plasma concentration; AUC = area under the curve; AUC<sub>norm</sub> = area under the curve normalised to the dose administered; SD = standard deviation.

No difference in fibrinogen activity was observed between males and females. There was no difference in the pharmacokinetics of FIBRYNA between adults and adolescents (12-17 years of age).

### 14 CLINICAL STUDIES

An interim analysis of an ongoing prospective, open-label, uncontrolled, multicentre clinical study was conducted in 13 patients with congenital fibrinogen deficiency (afibrinogenemia and hypofibrinogenemia), ranging in age from 13 to 53 years (2 adolescents, 11 adults). The data below describes 22 minor bleeding events (BEs), with minor bleeding defined as mild joint bleeding or superficial muscle, soft tissue, and oral bleeding. 15 (68%) BEs were spontaneous and 7 (32%) BEs were traumatic.

The median number of infusions for BEs was 1. Two (9%) BEs required 2 infusions. None of the BEs required more than 2 infusions. The median dose of FIBRYNA per infusion for treatment of all BEs was 58 mg/kg.

The treatment of all of the minor BEs studied was assessed for efficacy using a 4-point haemostatic efficacy scale. The scale was based on criteria such as bleeding cessation, changes in hemoglobin, and use of any other hemostatic means. Of 22 evaluable bleeding events, 21 (95%) were assessed as having a successful efficacy outcome (rating of good or excellent efficacy) by both the investigator and by an independent adjudication committee. For one BE, the investigator's assessment was missing. When considering only the first BE in each patient, all 10 BEs (100%) were assessed as having a successful efficacy outcome (rating of good or excellent efficacy) by both the investigator and the independent adjudication committee.
16 HOW SUPPLIED/ STORAGE AND HANDLING

How supplied:
FIBRYNA is supplied in a single-use bottle.

The following nominal dosage form is available:

<table>
<thead>
<tr>
<th>Carton NDC Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIBRYNA 1g</td>
</tr>
<tr>
<td>68982-347-01</td>
</tr>
</tbody>
</table>

- The actual potency of fibrinogen in mg is stated on each FIBRYNA carton and bottle.
- FIBRYNA is supplied in a package with a single-dose bottle of powder together with an Octajet transfer device and a particle filter.
- Components used in the packaging of FIBRYNA are not made with natural rubber latex.

Storage and Handling:
- Store FIBRYNA for up to 30 months at +2°C to +25°C (36°F to 77°F) from the date of manufacture.
- Do not use FIBRYNA beyond the expiration date printed on the carton and bottle.
- Do not freeze. Store in the original container to protect from light.
- After reconstitution, do not refrigerate or freeze the FIBRYNA solution. Use the reconstituted FIBRYNA solution immediately or within 4 hours after reconstitution.
- Dispose of any unused product or waste material in accordance with local requirements.

17 PATIENT COUNSELING INFORMATION

- Inform patients of the early signs of hypersensitivity or allergic reactions to FIBRYNA, including hives, chest tightness, wheezing, hypotension, and anaphylaxis (see Warnings and Precautions [5.1]). Advise them to notify their physician immediately if they experience any of these symptoms.

- Inform patients that blood clots with or without consequent obstruction of blood flow may occur with FIBRYNA. Any symptoms of blood clots such as unexplained chest and/or leg pain or swelling of the legs or arms, coughing up blood, shortness of breath, increased rate of breathing or unexplained symptoms related to the nervous system such as stroke or weakness following administration of FIBRYNA should be reported to their physician immediately (see Warnings and Precautions [5.2]).

- Inform patients that FIBRYNA is made from human plasma (part of the blood) and may contain infectious agents, e.g., viruses and, theoretically, the Creutzfeldt-Jakob Disease agent, that can cause disease. Explain the risk that FIBRYNA may transmit an infectious agent has been reduced by screening the plasma donors, by testing the donated plasma for certain virus infections, and by two processes demonstrated to inactivate and/or remove certain viruses during manufacturing (see Warnings and Precautions [5.3]). Symptoms of a possible virus infection include headache, fever, nausea, vomiting, weakness, malaise, diarrhea, or, in the case of hepatitis, jaundice.

Manufactured by:
Octapharma Pharmazeutika Produktionsges.m.b.H.
Oberlaer Strasse 235
A-1100 Vienna, Austria
U.S. License No. 1646

Distributed by:
Octapharma USA Inc.
121 River Street, Suite 1201
Hoboken, NJ 07030
Instructions for Use

FIBRYNA / fye bri' nah /
Fibrinogen (Human)

Read these instructions carefully before using FIBRYNA for the first time. The general guidelines for mixing and infusing FIBRYNA are listed below. If you are unsure of any of these steps, please contact the manufacturer before using FIBRYNA.

FIBRYNA is supplied as a powder. Before it can be infused, it must be mixed with sterile Water for Injection.
FIBRYNA is provided with the Octajet transfer device for reconstitution of the FIBRYNA powder in sterile Water for Injection, and a particle filter to filter the reconstituted solution before injection.

Instructions for Mixing FIBRYNA

1. Warm both the powder and sterile Water for Injection (sWFI) in their closed bottles to room temperature. This temperature should be maintained during reconstitution. If a water bath is used for warming, prevent water from 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 FIBRYNA bottle and the sWFI bottle to expose the central portion of the rubber stoppers. Clean the rubber stoppers with an alcohol swab and allow the rubber stoppers 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 package.

4. Take the Octajet in its outer package and invert it over the FIBRYNA bottle. Place the device while in the outer package onto the center of the FIBRYNA bottle until the clips of the product spike (colorless) are locked. While holding onto the FIBRYNA bottle, carefully remove the outer package from the Octajet, being careful not to touch the water spike (blue) and leave the Octajet attached firmly to the FIBRYNA bottle. (Fig. 1)

5. With the FIBRYNA bottle held firmly on a level surface, invert the sWFI 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 sWFI bottle. (Fig. 2)

6. Remove the distance ring (Fig. 3) and press the sWFI bottle down (Fig. 4). sWFI will flow into the FIBRYNA bottle.

7. When transfer of the sWFI is complete, gently swirl the FIBRYNA bottle until the powder is fully dissolved. To avoid foam formation, do not shake the bottle. The powder should be dissolved completely within approximately 5 to 10 minutes.
8. Turn the blue sWFI bottle connector (both directions possible) to bring the position markers together and remove the sWFI bottle together with the water spike (Fig. 5). Keep the FIBRYNA bottle upright to avoid leaking.

![Fig. 5](image)

9. Firmly connect the provided particle filter on the remaining Luer Lock on the FIBRYNA bottle (Fig. 6) and withdraw the solution through the particle filter into the syringe. (Fig. 7,8)

![Fig. 6](image) ![Fig. 7](image) ![Fig. 8](image)

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

**Instructions for Injecting FIBRYNA**

*For intravenous use only after reconstitution.*

1. Inspect the reconstituted FIBRYNA solution in the syringe for visible particulate matter and discoloration prior to administration. Do not use if particulate matter or discoloration are observed.
2. Do not administer FIBRYNA in the same tubing or container as other medications.
3. Clean the chosen injection site with an alcohol swab.
4. Attach a standard infusion set to the syringe. Insert the needle of the infusion set into the chosen vein.
5. Perform intravenous infusion. The rate of administration should be determined by the patient’s comfort level, at a recommended maximum rate of 5 mL per minute.
6. After infusing FIBRYNA, remove and properly discard the infusion set. After the infusion, remove the peel-off label containing the batch number from the FIBRYNA bottle, and place it in the log book for record keeping. Discard the empty bottle.

**Manufactured by:**
Octapharma Pharmazeutika Produktionsges.m.b.H.
Oberlaer Strasse 235
A-1100 Vienna, Austria
U.S. License No. 1646

**Distributed by:**
Octapharma USA, Inc.
Waterfront Corporate Center
121 River Street, Suite 1201
Hoboken, NJ 07030

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