Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

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

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Human Fibrinogen
Each bottle of FIBRYGA contains 2 g human fibrinogen. After reconstitution with 100 mL water for injections FIBRYGA contains approximately 20 mg/mL human fibrinogen.
The content of clottable protein is determined according to the European Pharmacopoeia for human fibrinogen.
Produced from the plasma of human donors.
Excipients with known effect: sodium up to 264 mg (11.5 mmol) per bottle.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder and solvent for solution for injection/infusion.
The powder is white or pale yellow and hygroscopic, also appearing as a friable mass.
The solvent is a clear and colourless liquid.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of bleeding episodes and peri-operative prophylaxis in patients with congenital hypo- or afibrinogenaemia with bleeding tendency.
As complementary therapy to management of uncontrolled severe haemorrhage in patients with acquired hypofibrinogenaemia in the course of surgical intervention.

4.2 Posology and method of administration

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.
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:
Dose (mg/kg body weight) = [Target level (g/L) - measured level (g/L)]
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:
Dose (mg/kg body weight) = [Target level (g/L) - measured level (g/L)]
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.
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.
For instructions on reconstitution of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability
In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.
Thromboembolism
There is a risk of thrombosis when patients, with either congenital or acquired deficiency, are treated with human fibrinogen particularly with high dose or repeated dosing. Patients given human fibrinogen should be observed closely for signs or symptoms of thrombosis.
In patients with a history of coronary heart disease or myocardial infarction, in patients with liver disease, in peri- or post-operative patients, in neonates, or in patients at risk of thromboembolic events or disseminated intravascular coagulation, the potential benefit of treatment with human plasma fibrinogen should be weighed against the risk of thromboembolic complications. Caution and close monitoring should also be performed.
Acquired hypofibrinogenaemia is associated with low plasma concentrations of all coagulation factors (not only fibrinogen) and inhibitors and so treatment with blood products containing coagulation factors should be considered. Careful monitoring of the coagulation system is necessary.
Allergic or anaphylactic-type reactions
If allergic or anaphylactic-type reactions occur, the injection/infusion should be stopped immediately. In case of anaphylactic shock, standard medical treatment for shock should be implemented.
Sodium Content
This medicinal product contains up to 264 mg sodium per bottle, equivalent to 13.2% of the WHO recommended maximum daily intake of 2 g sodium for an adult. To be taken into consideration by patients on a controlled sodium diet.
Virus safety
Standard measures to prevent infections resulting from the use of medicinal products prepared from human blood or plasma include selection of donors, screening of individual donations and plasma pools for specific markers of infection and the inclusion of effective manufacturing steps for the inactivation / removal of viruses. Despite this, when medicinal products prepared from human blood or plasma are administered, the possibility of transmitting infective agents cannot be totally excluded. This also applies to unknown or emerging viruses and other pathogens.
The measures taken are considered effective for enveloped viruses such as HIV, HBV and HCV, and for the non-enveloped virus HAV. 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 (fetal infection) and for individuals with immunodeficiency or increased erythropoiesis (e.g. haemolytic anaemia).
Appropriate vaccination (hepatitis A and B) should be considered for patients in regular/repeated receipt of human plasma-derived products.

Immunogenicity
In the case of replacement therapy with coagulation factors in other congenital deficiencies, antibody reactions have been observed, but there is currently no data with fibrinogen concentrate.

4.5 Interaction with other medicinal products and other forms of interaction

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

4.6 Fertility, pregnancy and lactation

Pregnancy
The safety of FIBRYGA for use in human pregnancy has not been established in controlled clinical trials. Clinical experience with fibrinogen products in the treatment of obstetric complications suggests that no harmful effects on the course of the pregnancy or health of the fetus or the neonate are to be expected.
Animal reproduction studies have not been conducted with FIBRYGA (see section 5.3). Since the active substance is of human origin, it is catabolised in the same manner as the patient's own protein. These physiological constituents of the human blood are not expected to induce adverse effects on reproduction or on the fetus.
Breastfeeding
It is unknown whether FIBRYGA is excreted in human milk. However, because of the nature of the substance, no effects on the breastfed newborn/infant are anticipated.
Thus, a decision must be made whether FIBRYGA therapy is indicated during breast-feeding taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.
Fertility
There are no data on fertility available.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Summary of the safety profile
There are no robust data on the frequency of adverse reactions from clinical trials with this product.

In clinical studies, the following adverse reactions have been reported: pyrexia, drug eruption, phlebitis and thrombosis.

The following adverse reactions have been reported for FIBRYGA and other fibrinogen concentrates:

MedDRA Standard System Organ Class	Undesirable effects	Frequency*
Immune system disorders:	Allergic or anaphylactic-type reactions Skin reactions	Unknown
Vascular disorders:	Thromboembolic episodes (including myocardial infarction and pulmonary embolism) (see section 4.4) Thrombophlebitis	Unknown
General disorders and administration site conditions:	Increase in body temperature (pyrexia)	Unknown

*Frequency unknown as it could not be calculated from the available data. Mild pyrexia and skin reaction were single occurrences during clinical studies. Allergic or anaphylactic-type reactions, thromboembolic episodes (including myocardial infarction and pulmonary embolism) and thrombophlebitis are class effects.

For safety in respect to transmissible agents, see section 4.4.

Paediatric population:
Twenty-six patients, 1 to <18 years of age, were included in the congenital fibrinogen deficiency safety analysis, of which 12 adolescents 12 to <18 years of age, 8 children 6 to <12 years of age and 6 children 1 to <6 years of age.
The overall safety profile does not differ between adults, adolescents and children.
There are no data on use of FIBRYGA in paediatric patients with acquired fibrinogen deficiency.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system:

HPRA Pharmacovigilance
Website: www.hpra.ie

4.9 Overdose

In order to avoid overdose, regular monitoring of the plasma level of fibrinogen during therapy is indicated (see 4.2).
In case of overdose, the risk of development of thromboembolic complications is enhanced.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antihaemorrhagics, fibrinogen, ATC code: B02BB01

Human fibrinogen (coagulation factor I), in the presence of thrombin, activated coagulation factor XIII (FXIIIa) and calcium ions, is converted into a stable and elastic three-dimensional fibrin haemostatic clot.

The administration of human fibrinogen provides an increase in plasma fibrinogen level and can temporarily correct the coagulation defect of patients with fibrinogen deficiency.

An open-label, prospective, randomised, controlled, two-arm cross-over single-dose pharmacokinetic phase 2 study in 22 patients with congenital fibrinogen deficiency (afibrinogaenemia) (see section 5.2) also evaluated the maximum clot firmness (MCF) as a surrogate marker for haemostatic efficacy (FORMA-01). MCF was determined by thromboelastometry (ROTEM) testing. For each patient, MCF was determined before (baseline) and one hour after the single-dose administration of FIBRYGA. MCF values were significantly higher after administration of FIBRYGA than at baseline (see the table below).

Table 1: Maximum clot firmness MCF [mm] (ITT population) n=22

Time point	Mean ± SD	Median (range)
Pre-infusion	0 ± 0	0 (0-0)
1 hour post-infusion	9.7± 3.0	10.0 (4.0-16.0)
Mean change (primary analysis)*	9.7 ± 3.0	10.0 (4.0-16.0)

MCF = maximum clot firmness; ITT = intention-to-treat.
*p < 0.0001 (95% confidence interval 8.37; 10.99)

A prospective, open label, uncontrolled, multicentre phase 3 study (FORMA-02) was conducted in 25 patients with congenital fibrinogen deficiency (afibrinogenaemia and hypofibrinogaenemia), ranging in age from 12 to 54 years (6 adolescents, 19 adults). This included the treatment of 89 bleeding episodes and 12 surgical procedures. There was significant change from baseline in the MCF as measured by ROTEM and fibrinogen plasma levels. The median dose of FIBRYGA per infusion for the treatment of bleeding episodes was 57.5 mg/kg and the median total dose was 59.4 mg/kg. The median total dose of FIBRYGA per surgery was 85.8 mg/kg. Overall haemostatic efficacy was rated as successful (rating of good or excellent efficacy) for 98.9% of the treated bleeding episodes and for 100% of the surgeries by an independent adjudication committee using an objective scoring system.

Another prospective, open label, uncontrolled, multicentre phase 3 study (FORMA-04) was conducted in 14 children with congenital fibrinogen deficiency (afibrinogenemia and hypofibrinogenemia), ranging in age from 1 to 10 years (6 <6 years of age and 8 between 6 and <12 years of age). This included the treatment of 10 bleeding episodes and 3 surgical procedures, as well as single dose pharmacokinetics. There was a significant change from baseline in the MCF as measured by ROTEM and fibrinogen plasma levels. The median dose of FIBRYGA per infusion for treatment of bleeding episodes was 70.2 mg/kg and the median total dose was 73.9 mg/kg. The median total dose of FIBRYGA per surgery was 108 mg/kg. Overall haemostatic efficacy was rated as successful (rating of good or excellent efficacy) for 100 % of the treated bleeding episodes and of the surgeries by an independent adjudication committee using an objective scoring system.

The prospective, randomised, controlled study FORMA-05 investigated the haemostatic efficacy and safety of FIBRYGA by comparison with cryoprecipitate as fibrinogen supplementation sources in patients developing acquired fibrinogen deficiency during cytoreductive surgery for the extensive abdominal malignancy pseudomyxoma peritonei. The study included 43 adult patients in the Per Protocol (PP) analysis set, 21 patients treated with FIBRYGA and 22 patients treated with cryoprecipitate. Intraoperative fibrinogen supplementation was performed pre-emptively (i.e. after 60-90 minutes in surgery, when excessive blood loss was observed, but before 2 litres of blood had been lost) with doses of 4 g of FIBRYGA or of 2 pools of 5 units of cryoprecipitate, repeated as needed. During the 7.8 ± 1.7 hours of surgery, 6.5 ± 3 g of FIBRYGA (89 ± 39 mg/kg BW) and 4.1 ±

2.2 pools of 5 units of cryoprecipitate were used, respectively. A median of 1 unit and 0.5 units RBC were administered intraoperatively to the patients treated with FIBRYGA and cryoprecipitate, respectively, with a median of 0 units RBC during the first 24 hours postoperatively in both groups (see the table below). No fresh frozen plasma or platelet concentrates were transfused during the study Haemostatic therapy based on fibrinogen supplementation was rated as successful for 100% of the surgeries in both groups by an independent adjudication committee using an objective scoring system.

Table 2: RBC* transfusion [units] intraoperatively and during the first 24 hours postoperatively (PP population)

Time frame	FIBRYGA group (n=21) Median (range)	Cryoprecipitate group (n=22) Median (range)
Intraoperatively	1 (0-4)	0.5 (0-5)
First 24 hours postoperatively	0 (0-2)	0 (0-2)

RBC = red blood cell concentrates; PP = per protocol.
*no transfusion of other allogeneic blood products, such as fresh frozen plasma or platelet concentrates, occurred

Paediatric population
In congenital fibrinogen deficiency, FIBRYGA was administered in two clinical studies (FORMA-02 and FORMA-04) in 20 patients from 1 to <18 years of age, of which 6 adolescents 12 to <18 years of age, 8 children 6 to <12 years of age and 6 children 1 to <6 years of age. Haemostatic efficacy was assessed as successful by an independent adjudication committee for all bleeding episodes treated (10 bleeding episodes in adolescents, 5 in children 6 to <12 years of age and 5 in children 1 to <6 years of age) and prophylaxis was also assessed as successful for the 4 surgeries performed in these patients (1 in adolescents and 3 in children 1 to <6 years of age).

5.2 Pharmacokinetic properties

Human fibrinogen is a normal constituent of human plasma and acts like endogenous fibrinogen. In plasma, the biological half-life of fibrinogen is 3–4 days. FIBRYGA is administered intravenously and is immediately available in a plasma concentration corresponding to the dosage administered.
An open-label, prospective, randomised, controlled, two-arm cross-over phase 2 study in 22 patients with congenital fibrinogen deficiency (afibrinogenemia), ranging in age from 12 to 53 years (6 adolescents, 16 adults), compared the single-dose pharmacokinetic properties of FIBRYGA with those of another commercially available fibrinogen concentrate in the same patients (FORMA-01). Each patient received a single intravenous 70 mg/kg dose of FIBRYGA and the comparator product. Blood samples were drawn to determine the fibrinogen activity at baseline and up to 14 days after the infusion. The pharmacokinetic parameters of FIBRYGA in the per protocol (PP) analysis (n=21) are summarised in the table below.

Table 3: Pharmacokinetic Parameters (n=21) for Fibrinogen Activity (PP population*)

Parameter	Mean ± SD	Range
Half-life [hr]	75.9 ± 23.8	40.0–157.0
C_{max} [mg/dL]	139.0 ± 36.9	83.0–216.0
AUC_{norm} for dose of 70 mg/kg [mg*hr/mL]	113.7 ± 31.5	59.7–175.5
Clearance [mL/hr/kg]	0.67 ± 0.2	0.4–1.2
Mean residence time [hr]	106.3 ± 30.9	58.7–205.5
Volume of distribution at steady state [mL/kg]	70.2 ± 29.9	36.9–149.1

*One patient excluded from the PP population because of receiving <90% of the planned dose of FIBRYGA and Comparator product
C_{max} = maximum plasma concentration; AUC_{norm} = area under the curve normalised to the dose administered; SD = standard deviation
The incremental in vivo recovery (IVR) was determined from levels obtained up to 4 hours post-infusion. The median incremental IVR was 1.8 mg/dL (range, 1.08–2.62 mg/dL) increase per mg/kg. The median IVR indicates that a dose of 70 mg/kg will increase the patient's fibrinogen plasma concentration by approximately 125 mg/dL.
Pharmacokinetics in specific populations
No statistically relevant difference in fibrinogen activity was observed between male and female study participants.
Paediatric population
Pharmacokinetic data in adolescents from 12 to less than 18 years of age was obtained in the FORMA-02 study. In the PP analysis, a small difference between the half-life for adolescents (n=5) and for adults (n=16) was observed, with 72.8 ± 16.5 hours as compared to 76.9 ± 26.1 hours, respectively. Clearance was almost identical in the two age groups, i.e., 0.68 ± 0.18 mL/hr/kg and 0.66 ± 0.21 mL/hr/kg, respectively.
The pharmacokinetic properties of FIBRYGA were further investigated in the FORMA-04 study in 13 children less than 12 years of age with congenital fibrinogen deficiency (afibrinogenaemia). Each patient received a single intravenous 70 mg/kg dose of FIBRYGA. The pharmacokinetic parameters of FIBRYGA are summarised in the table below. The median incremental IVR was 1.4 mg/dL (range, 1.3–2.1 mg/dL) increase per mg/kg.

Table 4: Pharmacokinetic Parameters (n=13) for Fibrinogen Activity

Parameter	Mean ± SD	Range
Half-life [hr]*	63.3 ± 12.0	45.6–91..6
Cmax [mg/dL]	107.2 ± 16.8	93.0–154.0
AUCnorm for dose of 70 mg/kg [mg*hr/mL]*	92.0 ± 20.0	69.7–134.2
Clearance [mL/hr/kg]*	0.8 ± 0.2	0.5–1.0
Mean residence time [hr]*	88.0 ± 16.8	63.6–126.7
Volume of distribution at steady state [mL/kg]*	67.6 ± 7.1	52.8–76.8

*Calculated in 10 of 13 patients, due to insufficient number of quantifiable values in 3 patients
IVR = in vivo recovery; Cmax = maximum plasma concentration; AUCnorm = area under the curve normalised to the dose administered; SD = standard deviation

5.3 Preclinical safety data

The safety of FIBRYGA has been demonstrated in several non-clinical safety pharmacology (cardiovascular effects, thrombogenic potential) and toxicology studies (acute toxicity, local tolerance). The non-clinical data reveal no special hazard for humans based on these studies. In the venous stasis test (Wessler test) FIBRYGA proved to be non-thrombogenic at doses up to 400 mg/kg body weight.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder
Arginine hydrochloride
Glycine
Sodium chloride
Sodium citrate dihydrate

Solvent
Water for Injections

6.2 Incompatibilities

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

6.3 Shelf life

3 years.

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. Partially used bottles should be discarded.

6.4 Special precautions for storage

Do not store above 25°C. Do not freeze. Keep the bottle in the outer carton to protect from light.
For storage conditions after reconstitution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Each pack of FIBRYGA 2 g contains:

- 2 g human fibrinogen in a 150 mL bottle (Type II glass) with a stopper (bromobutyl rubber) and a flip cap (aluminium)

- 100 mL solvent (water for injections) in a 100 mL vial (Type II glass) with a stopper (halobutyl rubber) and a flip cap (aluminium)
- 1 nextaro transfer device

6.6 Special precautions for disposal and other handling

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.



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.

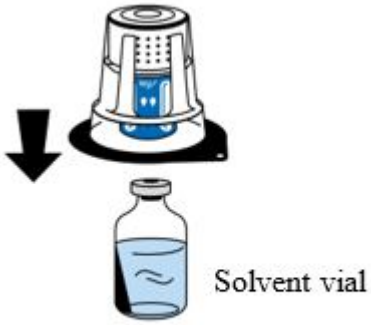


Fig. 2

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)

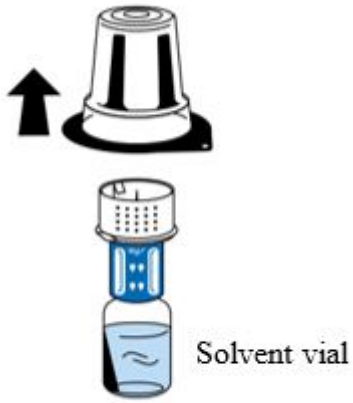


Fig. 3

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.

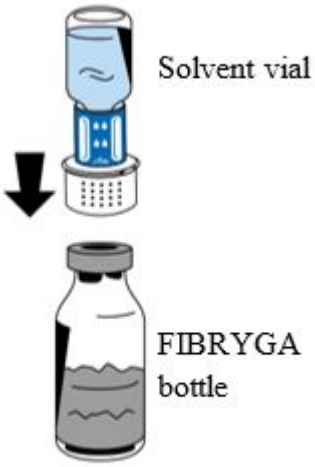


Fig. 4

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.

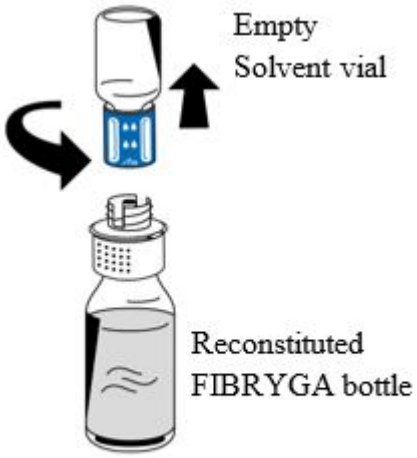


Fig. 5

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).



Fig. 6

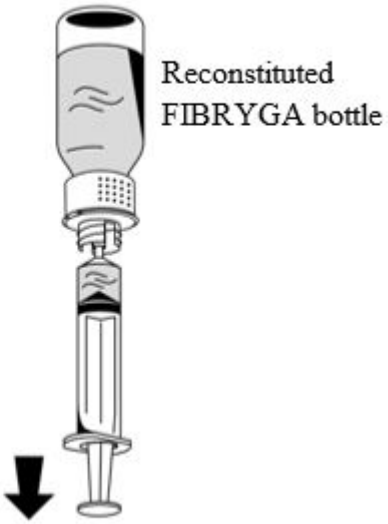


Fig. 7

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).

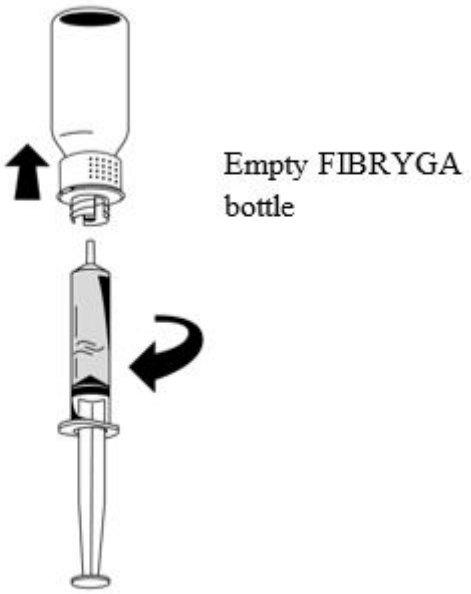


Fig. 8

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.

7 MARKETING AUTHORISATION HOLDER

Octapharma (IP)
Lennikse Baan 451
Anderlecht
Brussels-Capital Region
1070
Belgium

8 MARKETING AUTHORISATION NUMBER

PA2219/011/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 12th June 2026

10 DATE OF REVISION OF THE TEXT