fibryga®

Human Fibrinogen (Concentrate)

Adverse events should be reported. Reporting forms and information can be found at yellowcard.mhra.gov.uk.
Adverse events should also be reported to Octapharma by telephoning 01483 212 151.

octapharma

Prescribing information is available at the end of this presentation.

May 2022

Introduction

Considerations for choosing fibryga® for fibrinogen replacement:

- Commercial availability.
- Clinical indications.
- Fibrinogen content.
- Pack content.
- Storage flexibility.
- Method of reconstitution.
- Infusion speed.
- Stability.

Commercial situation

fibryga® is included on the 2022 Bleeding Disorders national framework covering England, Wales, Scotland and Northern Ireland - CM/PHS/19/5576.

fibryga® therapeutic indications[1]

fibryga® is the only fibrinogen concentrate with a dual indication in the UK[1,2,3]:

Congenital fibrinogen deficiency (CFD)

Treatment of bleeding and peri-operative prophylaxis in patients with congenital hypo- or afibrinogenaemia with bleeding tendency.

Acquired fibrinogen deficiency (AFD)

As complementary therapy to management of uncontrolled severe haemorrhage in patients with acquired hypofibrinogenaemia in the course of surgical intervention.

1. Fibryga SMPC. https://www.medicines.org.uk/emc/product/10315/smpc (Accessed April 2022).
2. Riastap SMPC. https://www.medicines.org.uk/emc/product/5909/smpc (Accessed April 2022).
3. Fibclot SMPC. https://www.medicines.org.uk/emc/product/2429/smpc (Accessed April 2022).

fibryga® at a glance: key features

Congenital indication	**Yes**
Acquired indication	**Yes**
Fibrinogen content/concentration	**1 g** **20 mg/mL**
Water for injection for reconstitution in pack	**Yes (50 mL)**
Reconstitution device in pack	**Yes**
Infusion rate – congenital	**5 mL/min**
Infusion rate - acquired	**10 mL/min**
Shelf-life and Storage conditions	**2 years** **Do not store above +25°C** **Do not freeze**
Post reconstitution stability	**24 hours at (maximum) +25°C**

Fibryga SMPC. https://www.medicines.org.uk/emc/product/10315/smpc (Accessed April 2022).

fibryga® at a glance: the pack

Patient Information Leaflet is in the pack

Powder bottle

50 mL water for injection (WFI)

Particle filter

Octajet® transfer device

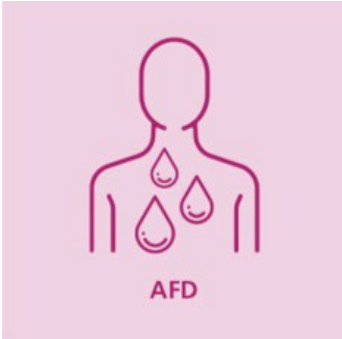
Fibryga SMPC. https://www.medicines.org.uk/emc/product/10315/smpc (Accessed April 2022).

Acquired fibrinogen deficiency and massive haemorrhage

Acquired hypofibrinogenaemia (low fibrinogen) is most frequently caused by haemodilution and consumption of clotting factors[1].

The aggressive replacement of fibrinogen has become one of the core principles of modern management of massive haemorrhage.[1]

Acquired hypofibrinogenaemia develops earlier than any other haemostatic anomaly in elective surgeries.[2]



1. Besser M.W. MacDonald SG. Acquired hypofibrinogenaemia: current perspectives. J Blood Med. 2016 Sep 26;7:217-225.
2. Hiippala S.T. et al. Hemostatic factors and replacement of major blood loss with plasma-poor red cell concentrates. Anesth Analg. 1995 Aug;81(2):360-5.

Considerations for fibrinogen replacement in surgical related acquired fibrinogen deficiency

Current therapeutic options with an acquired clinical indication:

fibryga®.[1]

Cryoprecipitate.[2]

1. Fibryga SMPC. https://www.medicines.org.uk/emc/product/10315/smpc (Accessed April 2022).
2. FACTSHEET: Cryoprecipitate. https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/22755/cryoprecipitate-factsheet-april-2021-v5.pdf (Accessed April2022).

Product comparison – composition and formulation

fibryga®[1]	Cryoprecipitate[2]	fibryga® compared to Cryoprecipitate
• 1g fibrinogen per bottle. • 50 mL WFI / 20 mg/mL. • Powder and solvent for reconstitution in 50mL WFI.	• 0.43 +/- 0.14 g fibrinogen /single bag and 1.67 +/- 0.27 g fibrinogen /pooled bag). • Single unit bag (20 - 60 mL) or pooled bag made up of five single units. (200 - 280 mL). • Frozen product requires thawing. • ABO blood group specific.	• Consistent fibrinogen content and infusion volume. • No need for freezing and thawing. • No need for blood grouping.

bag = unit

1. Fibryga SMPC. https://www.medicines.org.uk/emc/product/10315/smpc (Accessed April 2022).
2. Green L. et al. British Society of Haematology guidelines on the spectrum of fresh frozen plasma and cryoprecipitate products: their handling and use in various patient groups in the absence of major bleeding. British Journal of Haematology, 2018, 181, 54–67.

Product comparison – handling and infusion

fibryga®[1]	Cryoprecipitate	fibryga® compared to Cryoprecipitate
Reconstitution • Average reconstitution time <five minutes.[2] Infusion rate: • 10 mL/min - 600 mL/hr; five minutes per 1 g fibrinogen/bottle.[1]	Preparation[3] • Thaw at +33°C to +37°C. • Average thaw time 20 minutes (via water bath). Infusion rate[4]: • 10 - 20 mL/kg/hr; 30 - 60 minutes per five unit pooled bag.	• Reduction in time to prepare and infuse the required dose.[5]

1. Fibryga SMPC. https://www.medicines.org.uk/emc/product/10315/smpc (Accessed April 2022).
2. Schulz P, et al. Biochemical characterisation, stability and pathogen safety of a new fibrinogen concentrate (Fibryga®). Biologicals 2018.52:72-77.
3. Green L. et al. British Society of Haematology uidelines on the spectrum of fresh frozen plasma and cryoprecipitate products: their handling and use in various patient groups in the absence of major bleeding. British Journal of Haematology, 2018, 181, 54–67.
4. FACTSHEET: Cryoprecipitate. https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/22755/cryoprecipitate-factsheet-april-2021-v5.pdf (Accessed April2022).
5. Roy A, Stanford, S, Nunn, S, et al. Efficacy of fibrinogen concentrate in major abdominal surgery – A prospective, randomized, controlled study in cytoreductive surgery for pseudomyxoma peritonei. J Thromb Haemost. 2020; 18: 352– 363. https://doi.org/10.1111/jth.14665.

Product comparison - storage and stability

fibryga®[1]	Cryoprecipitate	fibryga® compared to Cryoprecipitate
• Do not store above +25°C. • Do not freeze. • Recommended for immediate use. • Stable for 24 hours at room temperature (RT) (max. +25°C) must not be frozen or refrigerated.	• Freeze at ≤ -25°C.[2] • Recommended for immediate use.[2] • Must be stored at RT and transfused within four hours of thawing.[2]	• Can be stored at place of need thus reducing time to start fibrinogen replacement. • If not reconstituted fibryga can be returned to storage. • Can be used within 24 hours of reconstitution increasing usage flexibility and reducing potential wastage.[3]

1. Fibryga SMPC. https://www.medicines.org.uk/emc/product/10315/smpc (Accessed April 2022).
2. FACTSHEET: Cryoprecipitate. https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/22755/cryoprecipitate-factsheet-april-2021-v5.pdf (Accessed April2022).
3. Callum J, Farkouh ME, Scales DC, et al. Effect of Fibrinogen Concentrate vs Cryoprecipitate on Blood Component Transfusion After Cardiac Surgery: The FIBRES Randomized Clinical Trial. Journal of the American Medical Association (JAMA). 2019;322(20):1966–1976. doi:10.1001/jama.2019.17312.

fibryga® key points for use in AFD in the surgical setting

- Indicated in AFD in severe surgical bleed management.[1]
- Consistent 1 g fibrinogen content.[1]
- The pack contains everything needed for reconstitution.[1]
- Five minute average reconstitution time.[2]
- Room temperature storage.[1]
- Post reconstitution stability of 24 hours at RT.[1]

1. Fibryga SMPC. https://www.medicines.org.uk/emc/product/10315/smpc (Accessed April 2022).
2. Schulz P, et al. Biochemical characterisation, stability and pathogen safety of a new fibrinogen concentrate (Fibryga®). Biologicals 2018.52:72-77.

Considerations for fibrinogen replacement in patients with congenital fibrinogen deficiency

Current concentrate choices with a congenital clinical indication:

Fibryga®[1]
Riastap®[2]
Fibclot®[3]

1. Fibryga SMPC. https://www.medicines.org.uk/emc/product/10315/smpc (Accessed April 2022).
2. Riastap SMPC. https://www.medicines.org.uk/emc/product/5909/smpc (Accessed April 2022).
3. Fibclot SMPC. https://www.medicines.org.uk/emc/product/2429/smpc (Accessed April 2022).

Fibrinogen concentrates comparison

	fibryga®[1]	Riastap®[2]	Fibclot®[3]
Fibrinogen content/concentration	1 g 20 mg/mL	1 g 20 mg/mL	1.5g 15 mg/mL
Water for injection for reconstitution in pack (volume)	Yes (50 mL)	Not provided	Yes (100 mL)
Reconstitution device in pack	Yes	Not provided	Yes
Storage conditions	Do not store above +25°C Do not freeze	Store in a refrigerator +2°C to +8°C Do not freeze	Do not store above +25°C Do not freeze
Post reconstitution stability	24 hours at +25°C (maximum)	Eight hours at room temperature (maximum +25°C)	Use immediately, do not store
Shelf life	Two years	Five years	Three years

1. Fibryga SMPC. https://www.medicines.org.uk/emc/product/10315/smpc (Accessed April 2022).
2. Riastap SMPC. https://www.medicines.org.uk/emc/product/5909/smpc (Accessed April 2022).
3. Fibclot SMPC. https://www.medicines.org.uk/emc/product/2429/smpc (Accessed April 2022).

fibryga® pack content

Patient Information Leaflet is in the pack

Powder bottle

50 mL water for injection (WFI)

Particle filter

Octajet® transfer device

Fibryga SMPC. https://www.medicines.org.uk/emc/product/10315/smpc (Accessed April 2022).

fibryga® congenital summary

- Approved for reimbursement with the national framework.
- 1 g fibrinogen. [1]
- Everything needed for reconstitution is in the pack.[1]
  - Alcohol swabs needed
- Five-minute reconstitution time.[2]
- Room temperature storage.[1]

1. Fibryga SMPC. https://www.medicines.org.uk/emc/product/10315/smpc (Accessed April 2022).
2. Schulz P, et al. Biochemical characterisation, stability and pathogen safety of a new fibrinogen concentrate (Fibryga®). Biologicals 2018.52:72-77.

Prescribing information

PRESCRIBING INFORMATION (PI): **fibryga®** (human fibrinogen)

Presentation:
Powder and solvent for solution for injection/infusion, available as 1 g human fibrinogen with 50 mL water for injection, equivalent to approximately 20 mg/mL human fibrinogen after reconstitution.

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.

Dosage and Administration: Treatment should be initiated under the supervision of a physician experienced in the treatment of coagulation disorders. **Dosage:** Dosage and duration of therapy depend on severity of disorder, location and extent of bleeding and patient's clinical condition. Determine (functional) fibrinogen level to calculate individual dosage. Determine amount and frequency of administration by regular measurement of plasma fibrinogen and continuous monitoring of clinical condition of patient and other replacement therapies used. In 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; maintain until haemostasis secured and above 0.5 g/L until wound healing complete. In case of surgical procedure or treatment of bleeding episode, the dose should be calculated as: Dose (mg/kg body weight) = [target level (g/L) – measured level (g/L)] divided by 0.018 (g/L per mg/kg body weight). Adapt subsequent doses and frequency based on patient's clinical status and laboratory results. Biological half-life of fibrinogen is 3-4 days thus, in absence of consumption, repeated treatment is not usually required. Given the accumulation that occurs with repeated administration for prophylactic use, dose and frequency should be determined by the therapeutic goals of the physician for a given patient. *Paediatric population:* In case of surgical procedure or treatment of bleeding episode, the dose in adolescents should be calculated according same formula as for adults above. Dose in children <12 years should be calculated as: Dose (mg/kg body weight) = [Target level (g/L) – measured level (g/L)] divided by 0.014 (g/L per mg/kg body weight). Subsequent posology should be adopted based on patient's clinical status and laboratory results. *Elderly:* Clinical studies did not include patients 65 years and over to provide conclusive evidence as to whether they would respond differently than younger patients.
2. Treatment of bleeding. *Bleeding in patients with congenital hypo- or afibrinogenaemia*: Treat bleeding episodes according to the formulas above for adult/adolescents and children, respectively, to achieve recommended target fibrinogen plasma level of 1 g/L; maintain until haemostasis secured. *Bleeding in patients with acquired fibrinogen deficiency*: In adults, administer 1-2 g initially, with subsequent infusions as required. In case of severe haemorrhage, larger amounts (4-8 g) may be required. In the paediatric population, dose according to body weight and clinical need, usually 20-30 mg/kg.

Method of Administration:
Intravenous infusion or injection. Patients with congenital hypo- or afibrinogenaemia: Administer slowly intravenously at ≤5 mL/min. Patients with acquired fibrinogen deficiency: Administer at ≤10 mL/min.

Contraindications:
Hypersensitivity to the active substance or any of the excipients.

Special Warnings and Precautions:
Traceability: Clearly record name and batch number of administered product to improve traceability. Thromboembolism: Particular risk with high dose or repeated dosing. Observe closely for signs or symptoms of thrombosis. In patients with predisposing risk factors, potential benefit of treatment should be weighed against risk of thromboembolic complications. Caution and close monitoring should be performed. Please consult the SmPC for further information. Allergic or anaphylactic-type reactions: If such reactions occur, stop injection/infusion immediately. In case of anaphylactic shock, implement standard medical treatment for shock. Sodium Level: Contains up to 132 mg sodium per bottle, equivalent to 6.6% of the WHO recommended maximum daily intake of 2 g sodium for an adult. Virus safety: Despite standard measures to prevent infections, possibility of transmitting infective agents, unknown or emerging viruses or other pathogens cannot be totally excluded. Preventative measures may be of limited value against nonenveloped viruses such as parvovirus B19. Parvovirus B19 infection may be serious for pregnant women and for individuals with immunodeficiency or increased erythropoiesis. Appropriate vaccination (HAV, HBV) should be considered for patients in regular/repeated receipt of human plasma-derived products. Fertility, pregnancy and lactation: Safety in 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 course of pregnancy or health of foetus or neonate are to be expected. Benefit of use during pregnancy must be evaluated given that clinical experience with fibrinogen concentrates is available but data from controlled clinical trials are missing. It is unknown whether fibryga® is excreted in human milk; however due to the nature of the substance, no effects on the breastfed newborn/infant are anticipated. Decision must be made in terms of benefit of breastfeeding for the child and benefit of therapy for the woman. There are no data on fertility available.

Undesirable Effects:
In clinical studies, the following have been reported: pyrexia, drug eruption, phlebitis and thrombosis. The following adverse reactions have been reported for this product and other fibrinogen concentrates (frequency unknown from available data): allergic or anaphylactic-type reactions; skin reactions; thromboembolic episodes (including myocardial infarction and pulmonary embolism); thrombophlebitis; pyrexia. Please refer to the SmPC for further information on adverse reactions.

Legal Category: POM
Pack Sizes and Basic NHS cost: 1 g £400.00
Marketing Authorisation Number: PL10673/0043
Marketing Authorisation Holder:
Octapharma Ltd, The Zenith Building, 26 Spring Gardens, Manchester, M2 1AB, United Kingdom.
Date of last revision: August-2021