FIBRYGA®

Introduction to Fibryga

Product Profile

Product Administration

Tools & Resources

FIBRYGA IN CANADA

APPROVED INDICATION

Acute bleeding episodes and perioperative prophylaxis in adult and pediatric patients with congenital afibrinogenemia and hypofibrinogenemia.

DOSAGE FORM

1 g powder

FIBRINOGEN CONTENT

~20 mg/ml after reconstitution with **50 ml** WFI

COMPOSITION

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

WFI=Water For Injection.
For complete Prescribing Information, please refer to the Canadian Fibryga® Product Monograph, August 10, 2018

Significant unmet needs in bleeding management

Current standard of care:

Cryoprecipitate

- 30-45 min to prepare
- Not purified; Variable fibrinogen content
- Not virally inactivated
- Requires blood type matching

Schulz P et al. Biochemical characterization, stability and pathogen safety of a new fibrinogen concentrate (Fibryga®). Biologicals 2017; https:///doi: 10.1016/j.biologicals.2017.12.003
Feedback from Fibryga advisory board meeting in 2017

FIBRYGA®: A MODERN FIBRINOGEN CONCENTRATE (FC)

Double virus inactivated- including COVID-19

High purity and fibrinogen activity

Robust global and Canadian clinical program

fibryga®

Fibryga® Canadian Product Monograph, August 10, 2018; Schulz et al. Biologicals 2018;52:72–77

PATHOGEN SAFETY- INCLUDING COVID-19

Dedicated 2-step pathogen removal

S/D treatment inactivates enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B (HBV) and hepatitis C virus (HCV)

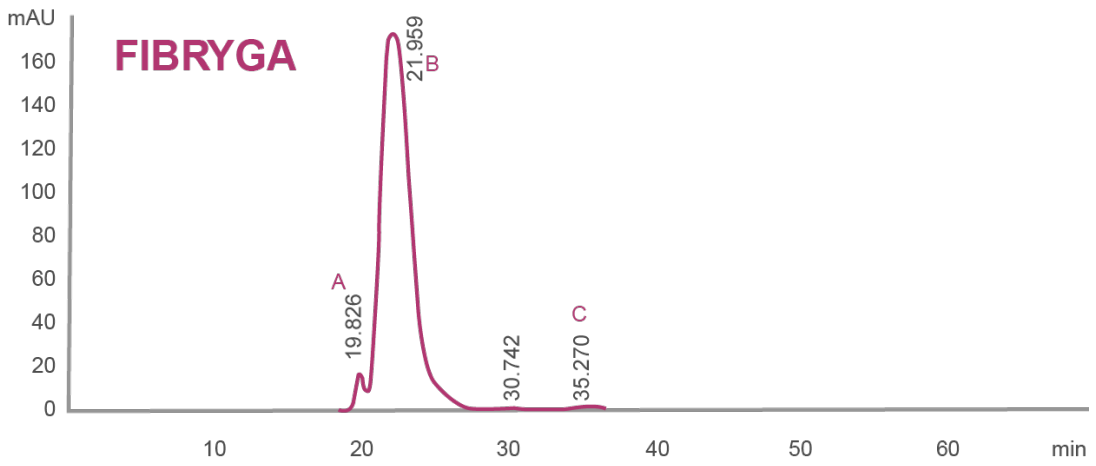
Nanofiltration (20 nm) for removal of both enveloped viruses and non-enveloped viruses—such as hepatitis A virus (HAV) and parvovirus B19, COVID-19 and potentially infectious prion protein

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.

Fibryga® Canadian Product Monograph, August 10, 2018

FIBRYGA SHOWS HIGH SPECIFIC ACTIVITIES OF ABOUT 98 ±7% CLOTTABLE PROTEIN[1], WITHOUT THE ADDITION OF PROTEIN STABILIZERS SUCH AS ALBUMIN[1,2]

Size exclusion chromatography of FIBRYGA[1]



Product composition in 1g vial[2,3]

		FIBRYGA®	RIASTAP®
Proteins	Human Fibrinogen	1000 mg	900-1300 mg
	Human Albumin	-	400-700 mg
Other excipients	L-Arginine hydrochloride	500 mg	375-660 mg
	Sodium chloride	300 mg	200-350 mg
	Sodium citrate	75 mg	50-100 mg
	Glycine	500 mg	-

Adapted from Fibryga and Riastap Product Monographs[2,3]

A: High molecular weight proteins **B:** Fibrinogen **C:** Albumin

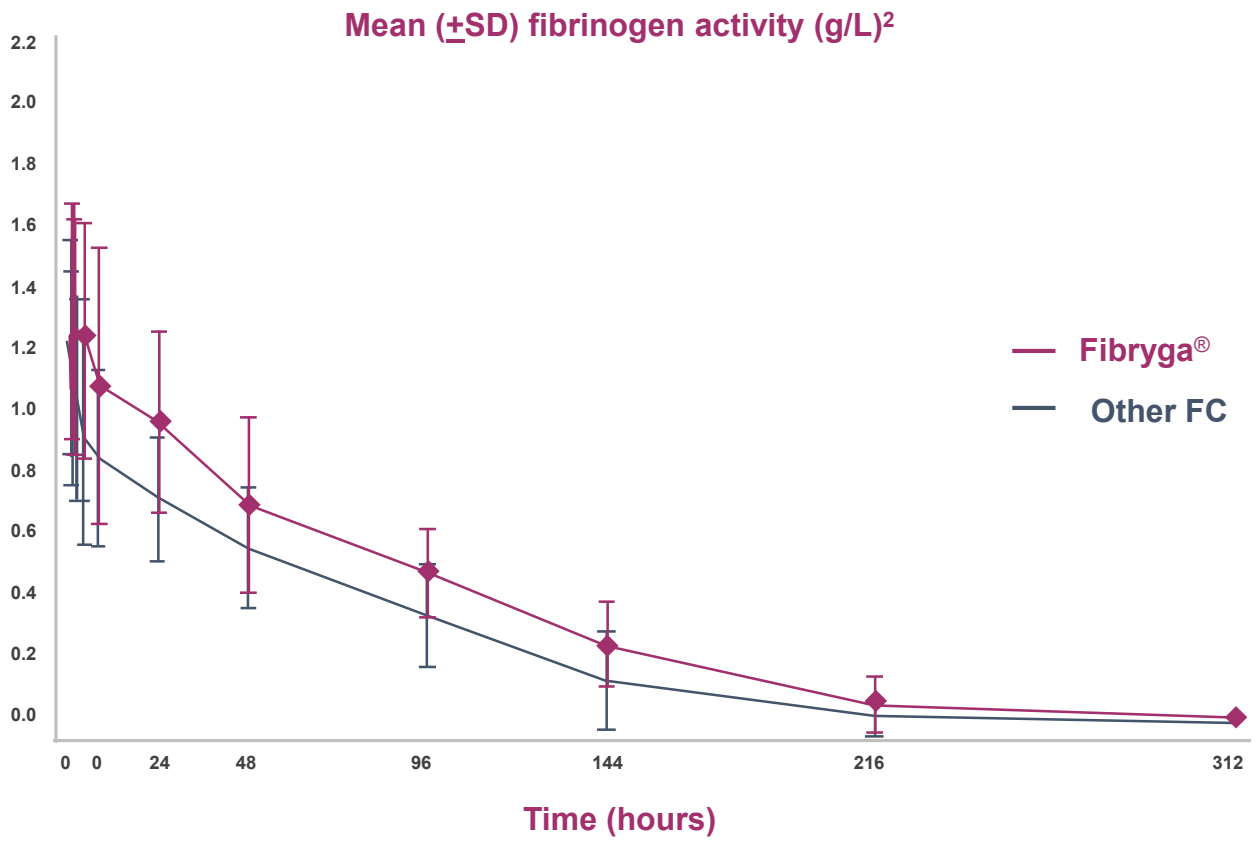
1. Schulz P et al. Biochemical characterization, stability and pathogen safety of a new fibrinogen concentrate (Fibryga®). Biologicals 2017; https://doi.org/10.1016/j.biologicals.2017.12.0031
2. Fibryga® Product Monograph, August 10, 2018
3. Riastap® Product Monograph, May 22, 2019

HIGHER BLOOD CONCENTRATIONS THAN COMPARATOR[2]

Fibryga® showed consistently larger AUCnorm than other FC (p=0.0002)[1,2]

Significantly lower product clearance[1,2]

Enhanced persistence of Fibryga® in blood plasma may be caused by a higher functional quality of protein structure and purity[1]



1.Fibryga® Product Monograph, August 10, 2018
2. Ross C et al. Pharmacokinetics, clot strength and safety of a new fibrinogen concentrate: randomized comparison with active control in congenital fibrinogen deficiency. J Thromb Haemost 2018; DOI: 10.1111/jth.13923.

EVIDENCE IN BOTH SURGICAL AND ACUTE BLEEDS IN CFD

CFD

FORMA-01	FORMA-02	FORMA-04
Phase II, comparative, pharmacokinetic (PK) study vs. existing FC	**Phase III** safety and efficacy study for on-demand treatment of bleeds and for preventing bleeding in surgery	**Phase IIIb** study to evaluate the efficacy and safety in acute bleeding in patients aged <12 years
COMPLETED	COMPLETED	COMPLETED

Lissitchkov T et al. Efficacy and safety of a new human fibrinogen concentrate in patients with congenital fibrinogen deficiency: an interim analysis of a phase III trial. Transfusion 2017; DOI: 10.1111/trf.14421

AVAILABLE THROUGH CBS PRODUCT ORDER FORM

FACTOR CONCENTRATES AND OTHER PLASMA PROTEIN PRODUCTS ORDER FORM

Canadian Blood Services

PAGE ____ **of** ____ **ALL ORDERS MUST BE FAXED**

Site: >

Hospital/Customer: _____ **Phone /Fax:** _____ **Date:** _____ **Time:** _____

City/Town: _____ **Requested By:** _____

Delivery Priority: **Routine** ☐ **ASAP** ☐ ***STAT** ☐ **[*STAT orders must be faxed and phoned]**

Delivery Mode: _____ **Date Needed:** _____ **Ship to Location:** _____

Comments: _____

Please indicate if substitution of specified products is acceptable: **Yes** ☐ **No** ☐

CBS Code	Product/Manufacturer	Vial Size	Vials/case	# of Vials	To Be Filled (For CBS Use Only)
Factor X					
*1000104822	Factor X P Behring, CSL Behring	600 IU	N/A		
Factor XI					
*U111000BP	Factor XI, Bio Products Laboratory	1000 IU	N/A		
Factor XIII					
1000106754	Corifact FXIII, CSL Behring	250 IU	10		
1000106755	Corifact FXIII, CSL Behring	1250 IU	10		
Recombinant Factor XIII					
1000106413	Tretten® rFXIII A-Subunit, Novo Nordisk	2500 IU	N/A		
Fibrinogen					
1000106414	RiaSTAP®, CSL Behring	1 g	8		
1000107397	Fibryga®, Octapharma	1 g	24		
Protein C					
*0PC0500IM	Ceprotin, Baxalta	500 IU	N/A		
*0PC1000IM	Ceprotin, Baxalta	1000 IU	N/A		

Conveniently order Fibryga® using the CBS *Factor Concentrates and Other Plasma Protein Products* Order Form

CBS: https://blood.ca/en/hospital-services/inventory-ordering/submitting-product-orders

WHAT COMES IN YOUR FIBRYGA® PACKAGE?

- **Fibryga® Powder Vial**
- **Octajet® Transfer Device**
- **Particle Filter**
- **Leaflet**

*Components used in Fibryga® packaging are latex-free

WATER FOR INJECTION (WFI) FOR THE RECONSTITUTION OF FIBRYGA®

WFI will be delivered by CBS alongside Fibryga®

WFI Specifications:

- Water for Injection USP (Sterile)
- 50 mL per vial
- DIN 00402257
- Code: L10010028
- 10 Vials (units) per package
- Shelf life: 48 months from date of production
- Storing: Store between 15-30ºC. Do not freeze
- Manufacturer: Omega Laboratory Ltd.

Omega Laboratories. Sterile Water for Injection: Medical Safety Data Sheet, December 21, 2015

Recommended dosing and infusion speed

INITIAL DOSING

RECOMMENDED TARGET FIBRINOGEN

Minor bleeding or minor surgery:
100 mg/dL

Major bleeding or major surgery:
150 mg/dL

RECOMMENDED DOSE

When baseline fibrinogen level is known:

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

When baseline fibrinogen level is not known:

60 mg/kg body weight

INFUSION SPEED

5 mL/min
(max)

HANDLING AND RECONSTITUTION

Easy to train

- Easy reconstitution using the Octajet® transfer device
- Quick to prepare
- Repetitive strain minimised

Fibryga Reconstitution Video

1. Fibryga® Canadian Product Monograph, August 10, 2018
2. CBS: Clinical Guide to Transfusion, Chapter 2 Blood Components: Sept. 2017

HELPFUL TIPS

DO

Use intravenously only

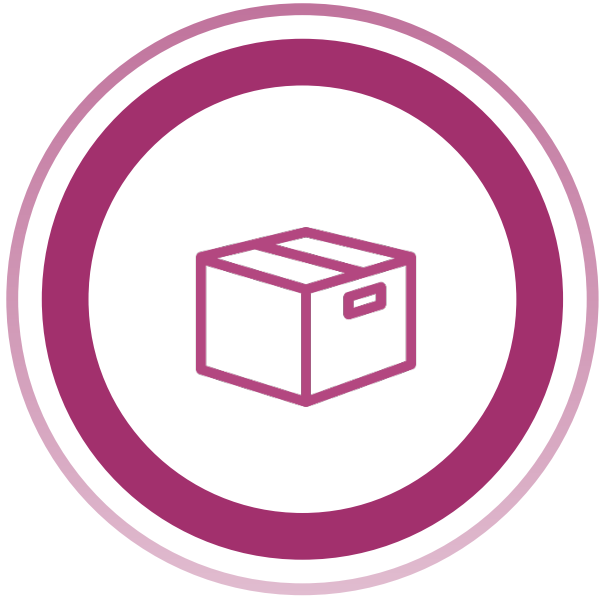
Use a separate intravenous line

DO NOT

Use solutions that are cloudy or have deposits

Mix with other medicinal products

STORAGE AND STABILITY AFTER RECONSTITUTION



Storage

Fibryga®: +2~25ºC

Other FC: +2-8ºC

Cryoprecipitate: -18ºC

Shelf Life

Fibryga®: 3 years

Other FC: 5 years

Cryoprecipitate: 1 year

Stability after Reconstitution

Fibryga®: 24h at +25ºC

Other FC: 8h at +25ºC

Cryoprecipitate: 4h

1. Fibryga® Canadian Product Monograph, August 10, 2018 ; 2. Schulz P et al. Biochemical characterization, stability and pathogen safety of a new fibrinogen concentrate (Fibryga®). Biologicals 2017; 3. Octapharma data on file. Pending publication; 4. RiaSTAP Canadian Product Monograph, May 22, 2019; 5. CBS Customer Letter # 2019-08: May 2019; 6. CBS: Clinical Guide to Transfusion, Chapter 2 Blood Components: Sept. 2017

FIBRYGA® VERSUS CRYOPRECIPITATE

		Fibryga®	Cryoprecipitate
Faster	**Reconstitution**	~5 minutes	~30-35 minutes
Less wastage	**Storage**	Room temperature or fridge	Frozen
	Stability after Reconstitution	24 hours at room temperature	Once thawed and pooled: 4 hours
Predictable volume	**Fibrinogen content**	Higher fibrinogen activity Standard dose (4 g): 4 g	Variability in inter-donor levels of fibrinogen content Standard dose (10 units): 2.85 (±0.88) g
	Consistency of other coagulation factors	Standardized levels of Factor VIII/VWF, FXIII and Fibronectin. No albumin	Variable amounts of additional coagulation factors such as Factor VIII/VWF, Factor XIII, Fibronectin and Platelet microparticles
Safety	**Pathogen Inactivation**	Pathogen inactivated	No pathogen inactivation
No impact on production of platelets	**Impact on platelet production**	None	Loss of 1 U of platelet per 1 U of cryoprecipitate

1. Schulz P et al. Biochemical characterization, stability and pathogen safety of a new fibrinogen concentrate (Fibryga®). Biologicals 2017; https://doi.org/10.1016/j.biologicals.2017.12.0031.
2. NAC Statement on Fibrinogen Concentrate, July 19, 2018 \

FAST RECONSTITUTION

RECONSTITUTION TOOLS

VIDEO

TEAR OFF SHEETS

DEMO KIT

Fibryga Reconstitution Video

Indications & 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.

Contraindications for FIBRYGA® are patients with severe immediate hypersensitivity reactions, including anaphylaxis to FIBRYGA® or its components.

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.

FIBRYGA® studies have included eight children (12-17 years). No data are available in patients below 12 years of age.

The safety of FIBRYGA® for use in human pregnancy and during lactation has not been established in controlled clinical trials.

Adverse events

No serious adverse reactions have been reported in clinical studies with FIBRYGA® to date

The most serious adverse reactions that may potentially be observed for FIBRYGA® are thromboembolic episodes and anaphylactic type reactions

The majority of the adverse events (AEs) were single instances (e.g., 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

References

1. Fibryga® Canadian Product Monograph, August 10, 2018.
2. Octapharma data on file
3. Schulz P et al. Biochemical characterization, stability and pathogen safety of a new fibrinogen concentrate (Fibryga®). Biologicals 2017; https://doi.org/10.1016/j.biologicals.2017.12.003.
4. Ross et al. Pharmacokinetics, clot strength and safety of a new fibrinogen concentrate: randomized comparison with active control in congenital fibrinogen deficiency. Journal of Thrombosis and Haemostasis, 16: 253–261
5. Haas T et al. Comparison of the efficacy of two human fibrinogen concentrates to treat dilutional coagulopathy in vitro. Br J Anaesth 2017
6. Laurens N et al. Fibrin structure and wound healing. J Thromb Haemost 2006; 4: 932–939
7. Lissitchkov T et al. Efficacy and safety of a new human fibrinogen concentrate in patients with congenital fibrinogen deficiency: an interim analysis of a phase III trial. Transfusion 2017; DOI: 10.1111/trf.14421
8. Kozek-Langenecker et al. Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology. Eur J Anaesthesiol. 2013; 30(6):270-382.
9. Mosesson MW et al. Fibrinogen and fibrin structure and functions. J. Thromb. Haemost 2005; 3(8):1894-1904
10. Omega Laboratories. Sterile Water for Injection: Medical Safety Data Sheet, December 21, 2015