**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
CHALLENGES WITH EXISTING FIBRINOGEN REPLACEMENT THERAPIES

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

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® Canadian Product Monograph, August 10, 2018; Sordi et al., Biologicals 2018;52:72-77
Dedicated 2-step pathogen removal

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 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\(^2,3\)

<table>
<thead>
<tr>
<th></th>
<th>FIBRYGA(^\circledR)</th>
<th>RIASTAP(^\circledR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human Fibrinogen</td>
<td>1000 mg</td>
<td>900-1300 mg</td>
</tr>
<tr>
<td>Human Albumin</td>
<td>-</td>
<td>400-700 mg</td>
</tr>
<tr>
<td>L-Arginine hydrochloride</td>
<td>500 mg</td>
<td>375-660 mg</td>
</tr>
<tr>
<td>Sodium chloride</td>
<td>300 mg</td>
<td>200-350 mg</td>
</tr>
<tr>
<td>Sodium citrate</td>
<td>75 mg</td>
<td>50-100 mg</td>
</tr>
<tr>
<td>Glycine</td>
<td>500 mg</td>
<td>-</td>
</tr>
</tbody>
</table>

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

2. Fibryga® Product Monograph, August 10, 2018  
3. Riastap® Product Monograph, May 22, 2019
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\(^1\)
EVIDENCE IN BOTH SURGICAL AND ACUTE BLEEDS IN CFD

CFD

**FORMA-01**
Phase II, comparative, pharmacokinetic (PK) study vs. existing FC

**FORMA-02**
Phase III safety and efficacy study for on-demand treatment of bleeds and for preventing bleeding in surgery

**FORMA-04**
Phase IIIb study to evaluate the efficacy and safety in acute bleeding in patients aged <12 years

COMPLETED

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

<table>
<thead>
<tr>
<th>CBS Code</th>
<th>Product/Manufacturer</th>
<th>Vial Size</th>
<th>Vials/case</th>
<th># of Vials</th>
<th>To Be Filled (For CBS Use Only)</th>
</tr>
</thead>
<tbody>
<tr>
<td>*1000104822</td>
<td>Factor X Fehling, CSL Behring</td>
<td>600 IU</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Factor XI</td>
<td>F111000BP</td>
<td>1000 IU</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Factor XIII</td>
<td>1000106754</td>
<td>250 IU</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1000106755</td>
<td>Prokarell, CSL Behring</td>
<td>1250 IU</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recombinant Factor XIII</td>
<td>1000106413</td>
<td>2500 IU</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>1000106414</td>
<td>1 g</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1000107367</td>
<td>Fibryga, Octapharma</td>
<td>1 g</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein C</td>
<td>*OPC5000IM</td>
<td>500 IU</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>*OPC1000IM</td>
<td>Capron, Basella</td>
<td>1000 IU</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Available through CBS Product Order Form

FIBRYGA®: PACKAGE CONTENTS

WHAT COMES IN YOUR FIBRYGA® PACKAGE?

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

*Components used in Fibryga® packaging are latex-free
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 15-30°C. Do not freeze
- Manufacturer: Omega Laboratory Ltd.
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:
  \[
  \text{Dose (mg/kg body weight)} = \frac{[\text{Target level (mg/dL)} - \text{measured level (mg/dL)}]}{1.8 \text{ (mg/dL per mg/kg body weight)}}
  \]
- When baseline fibrinogen level is not known:
  60 mg/kg body weight

INITIAL DOSING

INFUSION SPEED

5 mL/min (max)
FIBRYGA®

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
**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

## Fibryga® Cryoprecipitate

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

### Notes

2. NAC Statement on Fibrinogen Concentrate, July 19, 2018
FIBRYGA®: RESOURCES
FAST RECONSTITUTION

RECONSTITUTION TOOLS

VIDEO
TEAR OFF SHEETS
DEMO KIT

Fibryga Reconstitution Video
FIBRYGA®: IMPORTANT INFORMATION

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

2. Octapharma data on file