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Teleflex Circular of Information

For the Use of EZPLAZ™ Freeze Dried Plasma

This Circular of Information is an extension of container labels. Federal law prohibits dispensing EZPLAZ™ Freeze Dried Plasma described in this circular without a prescription.

Manufactured by:

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EZPLAZ™ Freeze Dried Plasma

Description

EZPLAZ™ Freeze Dried Plasma (FDP) is a lyophilized plasma derived from single-donor human fresh frozen plasma (FFP), intended for reconstitution and intravenous or intraosseous transfusion. EZPLAZ™ FDP contains plasma proteins, including all coagulation factors. EZPLAZ™ FDP stability studies demonstrate retention of clinically meaningful coagulation factors at 2-25 C / 36-77 F for up to 12 months (see Table 1 and Table 2). EZPLAZ™ FDP is provided as blood groups AB or A, with low titer anti-B (< 1:200 by saline tube method). In the emergency treatment of hemorrhage or coagulopathy, group A and group AB EZPLAZ™ FDP may be administered to any patient prior to determining their ABO blood group. After reconstitution, the pH of EZPLAZ™ FDP ranges from 6.5 to 7.5.

Each EZPLAZ™ FDP unit is manufactured from approximately 270 mL of FFP collected from a male volunteer donor at U.S. licensed blood establishments. The exclusive use of male donors reduces the risk of transfusion-related acute lung injury (TRALI), because the unit is less likely to contain anti-human leukocyte antigen (HLA) antibodies.

Donor screening and infectious disease testing are performed in accordance with 21 CFR §630.10 (donor eligibility) and 21 CFR §610.40 (testing for relevant transfusion-transmitted infections).

Refer to AABB's Circular of Information for more information about Required Testing of Blood Donations in U.S. licensed blood establishments.

Actions

EZPLAZ™ FDP serves as a source of plasma proteins for patients who are deficient in or have defective plasma proteins.

Indications

EZPLAZ™ Freeze Dried Plasma (FDP) is indicated for transfusion in adults when plasma is required and other plasma products are not available.

Indications include:

- Management of preoperative or bleeding patients who require replacement of multiple plasma coagulation factors [e.g., liver disease, disseminated intravascular coagulation (DIC)]
- Patients undergoing massive transfusion who have clinically significant coagulation deficiencies
- Patients taking warfarin who are bleeding or need to undergo an invasive procedure before vitamin K could reverse the warfarin effect or who need only transient reversal of warfarin effect

Contraindications

Do not use EZPLAZ™ FDP:

- In patients with history of hypersensitivity to fresh frozen plasma (FFP), liquid plasma or to plasma-derived products including any plasma proteins
- In patients with IgA deficiency

Dosage and Administration

For intravenous (IV) and/or intraosseous (IO) use only. EZPLAZ™ FDP should be infused immediately after reconstitution. Infusion should be completed as soon as possible and within 4 hours when held at the recommended storage temperature. Discard any EZPLAZ™ FDP that is not infused within 4 hours after reconstitution.

Compatibility

EZPLAZ™ FDP is available as group AB and group A.

Select the EZPLAZ™ FDP product that is compatible with the recipient's ABO blood group (i.e., plasma unit's compatibility with recipient's red blood cells).

In the emergency treatment of hemorrhage or coagulopathy, either group A or group AB EZPLAZ™ FDP may be used prior to determining the recipient's ABO blood group.

Dose

The dose or volume to transfuse depends on the clinical situation and patient size; clinical decisions may be guided by laboratory and/or point of care assays of coagulation function, if available.

Administration

EZPLAZ™ FDP is available in a packaged kit that includes commercially available finished products:

- One (1) unit of EZPLAZ™ FDP
- One (1) bag containing 250 mL of USP grade Sterile Water for Injection (SWFI)
- One (1) sterile Fluid Transfer Set
- One (1) sterile Blood Transfusion Set;

EZPLAZ™ FDP must be transfused through the sterile Blood Transfusion Set provided in the kit which contains a 170-micron filter designed to remove clots and cellular aggregates.

EZPLAZ™ FDP is supplied as a powder and is reconstituted with sterile water for injection immediately before use to form an injectable preparation. When reconstituted, the volume of EZPLAZ™ FDP is equivalent to 270 mL of plasma.

The following transfusion safety instructions apply to administration of EZPLAZ™ FDP:

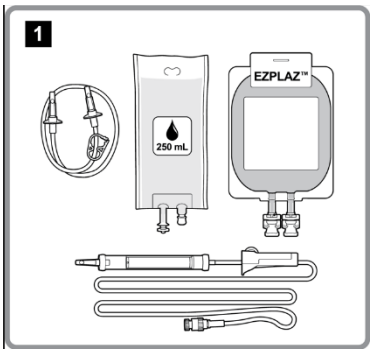
The intended recipient and the blood container must be properly identified before the transfusion is started.

Periodic observation and recording of vital signs should occur before, during, and after the transfusion to identify suspected adverse reactions.

If a transfusion reaction occurs, the transfusion must be discontinued immediately, and appropriate therapy initiated.

Specific information and instructions concerning possible adverse reactions should be provided to the patient or a responsible caregiver when direct medical observation or monitoring of the patient will not be available after transfusion.

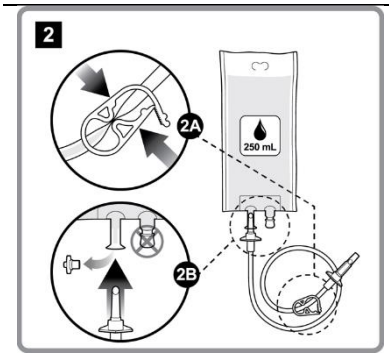
EZPLAZ™ FDP is reconstituted in the following manner using an aseptic technique and universal precautions:



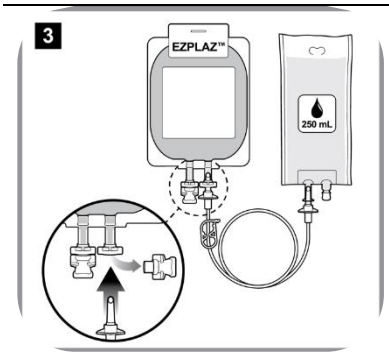
Using the tear notch, open the foil pouch and remove the EZPLAZ™ FDP unit.

Remove the outer packaging for the SWFI, Fluid Transfer Set (Transfer Set), and Blood Transfusion Set (Blood Set). Keep all spike protectors in place to maintain sterility.

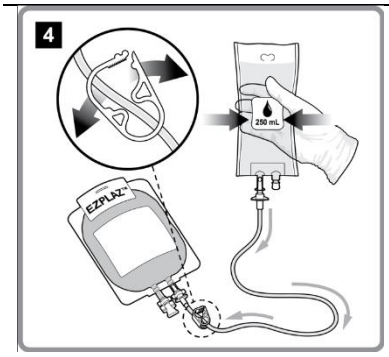
Inspect all items for signs of damage or breakage; **DO NOT USE** if damage is evident.



Slide the pinch clamp on the Transfer Set towards one end of the tubing. Close the pinch clamp completely [Fig. 2A].
Remove the SWFI port cap. Remove the spike protector farthest from the pinch clamp and firmly insert the spike into the SWFI port [Fig. 2B]. Press firmly until the spike pierces the membrane.
DO NOT prime the Transfer Set.
DO NOT touch the exposed Transfer Set spike or SWFI spike port.



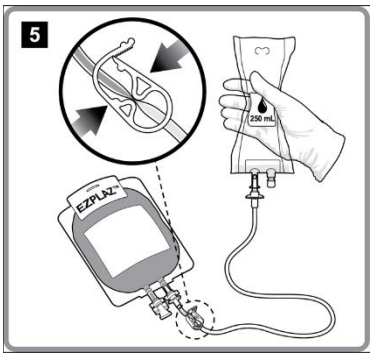
Remove either cap on the EZPLAZ™ FDP unit, then remove the protector for the remaining Transfer Set spike and firmly insert the spike into the EZPLAZ™ FDP spike port.
DO NOT touch the exposed Transfer Set spike or EZPLAZ™ FDP unit spike port.



Open the tubing clamp to transfer SWFI into the EZPLAZ™ FDP unit.

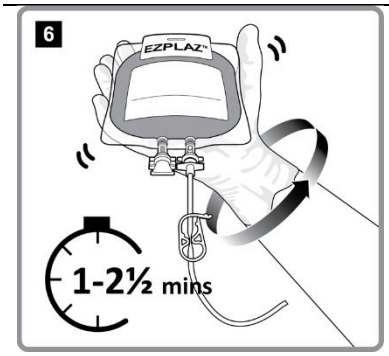
To aid fluid transfer, elevate the SWFI bag above the EZPLAZ™ FDP unit and gently squeeze the SWFI bag.

Transfer ALL the fluid from the SWFI bag into the EZPLAZ™ FDP unit.



Close the clamp completely between the EZPLAZ™ FDP unit and SWFI bag after fluid is transferred to prevent back-flow.

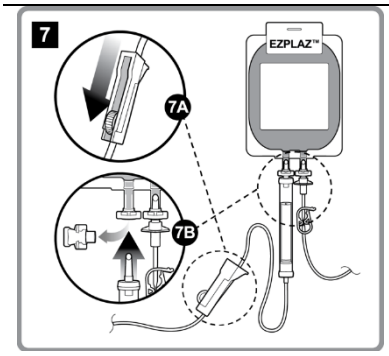
DO NOT disconnect the SWFI bag from the EZPLAZ™ FDP unit.



Gently agitate the EZPLAZ™ FDP unit in a circular motion by hand for about a minute; occasionally flip the EZPLAZ™ FDP unit while agitating. To minimize foaming, avoid vigorous shaking.

Visually inspect every 15 seconds to see if the powder has dissolved. If dried particles are still present, continue agitating for up to 2.5 minutes (150 seconds). The reconstituted product may develop some foam during reconstitution, which will dissipate with time. Unit should be discarded if reconstitution time is longer than 2.5 minutes.

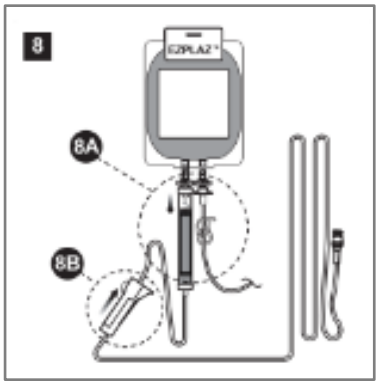
Note: Reconstituted EZPLAZ™ FDP is a near uniform, cloudy liquid.



Close the roller clamp on the Blood Set [Fig. 7A].

Remove the cap from the remaining spike port on the EZPLAZ™ FDP unit. Remove the spike protector of the Blood Set and insert into the EZPLAZ™ FDP spike port [Fig 7B].

DO NOT touch the exposed Blood Set spike or EZPLAZ™ FDP unit spike port.



Fill the drip chamber of the Blood Set until the filter is completely covered. Maintain fluid level above the filter during infusion [Fig. 8A].

Prime the line by slowly opening roller clamp and allow fluid to fill tubing [Fig. 8B].

If flow is blocked or restricted, DO NOT use EZPLAZ™ FDP unit.

Close roller clamp and ensure air is expelled. Repeat prime if necessary.

After establishing IV/IO vascular access, remove the protective cap from the distal end of the Blood Set and connect the Blood Set tubing. Open the Blood Set roller clamp and administer EZPLAZ™ FDP. Monitor the drip chamber for flow.

Infuse until bag is empty and/or drip chamber shows no more flow. Discard all kit components using appropriate biohazard protocols.

Additives

No medications or solutions may be added to EZPLAZ™ FDP or infused through the same administration tubing simultaneously, except for 0.9% Sodium Chloride Injection, United States Pharmacopeia (USP).

Lactated Ringer's Injection USP or other solutions containing calcium should never be added to or infused through the same tubing with blood or blood components containing citrate.

Warnings and Precautions

Warning: The risk of transmitting infectious agents is present. Careful donor selection and available laboratory tests do not eliminate the hazard.

As with other licensed blood products, EZPLAZ™ FDP may cause adverse events known to be associated with transfusion of blood products. For additional information regarding Warnings and Precautions associated with transfusion of blood products, refer to the AABB Circular of Information, Section: *Side Effects and Hazards for Whole Blood and Blood Components*.

The AABB Circular provides further details on potential transfusion-related adverse reactions, including hemolytic reactions, alloimmunization, transfusion-related acute lung injury (TRALI), transfusion-associated circulatory overload (TACO), allergic and anaphylactic reactions, and metabolic complications (e.g., citrate toxicity).

Hemolytic Transfusion Reactions

Hemolytic transfusion reactions can occur if the ABO groups of the donor and the recipient are incompatible. EZPLAZ™ FDP is provided as blood group AB or A with low titer anti-B (<

1:200 by saline tube method). Select EZPLAZ™ FDP for use based on the recipient's ABO group. In the emergency treatment of hemorrhage or coagulopathy, group A and group AB EZPLAZ™ FDP may be used prior to determining the recipient's blood group.

Transfusion-Related Acute Lung Injury (TRALI)

To mitigate the risk of TRALI, EZPLAZ™ FDP is manufactured from FFP donated by male donors only.

Infection Risk from Human Plasma

Because EZPLAZ™ FDP is made from human plasma, it may carry a risk of transmitting infectious agents, e.g., viruses, bacteria, and theoretically the variant Creutzfeldt-Jakob disease (vCJD) agent.

Hypersensitivity Reactions

Hypersensitivity reactions, including anaphylaxis, may occur. Discontinue the transfusion if signs or symptoms of hypersensitivity occur and treat appropriately.

Specific Therapies

EZPLAZ™ FDP may be less effective in correcting certain coagulopathies when therapies targeting specific coagulation factor deficiencies or anticoagulant effects are available. In such situations, clinicians should consider the use of targeted therapies, when clinically appropriate, including vitamin K for urgent vitamin K antagonist reversal, fibrinogen-containing products for hypofibrinogenemia, specific coagulation factor concentrates, or specific reversal agents for non-vitamin K antagonist anticoagulants. Selection of therapy should be based on the patient's clinical condition, urgency of correction, and availability of alternative treatments.

Volume Expansion

EZPLAZ™ FDP is not intended for routine volume expansion. When administered in the absence of a documented coagulation factor deficiency or plasma protein deficiency, the expected clinical benefit may be limited, and alternative volume expanders are generally more appropriate. Clinicians should consider alternative therapies based on the patient's clinical needs.

Elevated INR

Transfusion of EZPLAZ™ FDP may not result in a clinically meaningful correction of minimally elevated international normalized ratio (INR) values. In these situations, the likelihood of achieving clinically significant hemostatic benefit may be low, and alternative management strategies should be considered based on the patient's overall clinical condition.

Adverse Reactions

Serious adverse events or adverse drug reactions were not observed in the Phase 1 clinical trial; however, it is expected that, because EZPLAZ™ FDP is manufactured from FFP, adverse events associated with the use of FFP could occur.

All adverse events related to transfusion, including possible bacterial contamination of blood or a blood component, infection, or suspected disease transmission, must be reported to the transfusion service according to its local protocol.

Storage and Handling

Product Kit Before Reconstitution

Store kit at 2-25 C / 36-77 F for up to the expiration date printed on the label. Do not freeze. Protect from moisture. Do NOT open the EZPLAZ™ FDP foil pouch until the time of reconstitution. Discard kit after the expiration date on the label.

Reconstituted Product

Reconstitute product according to instructions in Administration. Infuse within 4 hours after reconstitution. Do not refrigerate. Do not freeze. Discard unused reconstituted product after 4 hours.

Reporting Adverse Reactions

To report SUSPECTED ADVERSE REACTIONS, contact Teleflex at 1-866-246-6990 and FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

Table 1: Coagulation Protein Levels in FFP and FDP at the time of Manufacture through 6 and 12 Months Storage at 4°C

Analyte	Result After Lyophilization (Mean ± SD [a])		Result After 6 and 12 Months Storage (Mean ± SD [b])		% Change, FDP Compared to FFP	
	FFP	FDP, T_0	FDP, T_{6M} (4°C Storage)	FDP, T_{12M} (4°C Storage)	FDP, T_0	FDP, T_{12M} (4°C Storage)
FII (IU/dL)	93.7 ± 10.4	86.2 ± 9.7	86.2 ± 9.7	86.2 ± 9.7	8	8
FV (IU/dL)	99.5 ± 16.1	92.0 ± 15.7	88.3 ± 15.7	89.2 ± 15.7	8	10
FVII (IU/dL)	97.9 ± 20.9	92.4 ± 19.6	89.6 ± 19.6	86.9 ± 19.6	6	11
FVIII (IU/dL)	128.7 ± 23.6	108.4 ± 21.4	98.6 ± 21.4	100.8 ± 21.4	16	22
FIX (IU/dL)	120.5 ± 18.4	108.6 ± 17.8	105.3 ± 17.8	102.1 ± 17.8	10	15
FX (IU/dL)	90.6 ± 13.5	86.4 ± 14.5	85.5 ± 14.5	84.7 ± 14.5	5	7
FXI (IU/dL)	93.1 ± 16.6	83.9 ± 15.2	83.9 ± 15.2	83.9 ± 15.2	10	10
FXII (IU/dL)	104.0 ± 22.9	97.3 ± 21.1	96.3 ± 21.1	96.3 ± 21.1	6	7
Fibrinogen (mg/dL)	352 ± 62	338 ± 61	331 ± 61	331 ± 61	4	6
Antithrombin (IU/dL)	94 ± 10	86 ± 10	85 ± 10	86 ± 10	9	9
Protein C (IU/dL)	98 ± 17	91 ± 16	91 ± 16	91 ± 16	7	7
Protein S (IU/dL)	106.6 ± 18.4	100.6 ± 16.6	97.6 ± 16.6	91.5 ± 16.6	6	14

vWF Activity (IU/dL)	142.2 ± 46.3	130.7 ± 40.3	126.8 ± 40.3	121.6 ± 40.3	8	14
vWF Antigen (IU/dL)	150.3 ± 44.9	142.4 ± 41.8	138.1 ± 41.8	138.1 ± 41.8	5	8

[a] Mean and SD values from individually tested plasma units pre- and post- lyophilization
[b] Mean values based on percent change observed in pooled stability batches tested over shelf-life. SD values assumed based on the individually tested FDP units at T_0
Notes:
Additional 4-hour post-reconstitution change of up to 12% has been observed for Factor VIII. Remaining factors have a post-reconstitution change of < 5% at 4 hours.
See Storage and Handling for allowed temperature ranges and durations.

Table 2: Coagulation Protein Levels in FFP and FDP at the time of Manufacture through 6 and 12 Months Storage at 25°C

Analyte	Result After Lyophilization (Mean ± SD [a])		Result After 6 and 12 Months Storage (Mean ± SD [b])		% Change, FDP Compared to FFP	
	FFP	FDP, T_0	FDP, T_{6M} (25°C Storage)	FDP, T_{12M} (25°C Storage)	FDP, T_0	FDP, T_{12M} (25°C Storage)
FII (IU/dL)	93.7 ± 10.4	86.2 ± 9.7	79.3 ± 9.7	71.5 ± 9.7	8	24
FV (IU/dL)	99.5 ± 16.1	92.0 ± 15.7	79.1 ± 15.7	70.8 ± 15.7	8	29
FVII (IU/dL)	97.9 ± 20.9	92.4 ± 19.6	84.1 ± 19.6	77.6 ± 19.6	6	21
FVIII (IU/dL)	128.7 ± 23.6	108.4 ± 21.4	85.6 ± 21.4	78.0 ± 21.4	16	39
FIX (IU/dL)	120.5 ± 18.4	108.6 ± 17.8	91.2 ± 17.8	81.5 ± 17.8	10	32
FX (IU/dL)	90.6 ± 13.5	86.4 ± 14.5	76.9 ± 14.5	67.4 ± 14.5	5	26
FXI (IU/dL)	93.1 ± 16.6	83.9 ± 15.2	78.0 ± 15.2	78.0 ± 15.2	10	16
FXII (IU/dL)	104.0 ± 22.9	97.3 ± 21.1	80.8 ± 21.1	72.0 ± 21.1	6	31
Fibrinogen (mg/dL)	352 ± 62	338 ± 61	301 ± 61	277 ± 61	4	21
Antithrombin (IU/dL)	94 ± 10	86 ± 10	83 ± 10	80 ± 10	9	15
Protein C (IU/dL)	98 ± 17	91 ± 16	87 ± 16	86 ± 16	7	12
Protein S (IU/dL)	106.6 ± 18.4	100.6 ± 16.6	84.5 ± 16.6	73.4 ± 16.6	6	31
vWF Activity (IU/dL)	142.2 ± 46.3	130.7 ± 40.3	103.3 ± 40.3	85.0 ± 40.3	8	40
vWF Antigen (IU/dL)	150.3 ± 44.9	142.4 ± 41.8	129.6 ± 41.8	121.0 ± 41.8	5	20

[a] Mean and SD values from individually tested plasma units pre- and post- lyophilization
[b] Mean values based on percent change observed in pooled stability batches tested over shelf-life. SD values assumed based on the individually tested FDP units at T_0
Notes:
Additional 4-hour post-reconstitution change of up to 12% has been observed for Factor VIII. Remaining factors have a post-reconstitution change of < 5% at 4 hours.
See Storage and Handling for allowed temperature ranges and durations.

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