Proposed Professional Information

SCHEDULING STATUS S4

PROPRIETARY NAME (AND DOSAGE FORM)

Bioplasma FDP (Powder for solution for IV infusion)

COMPOSITION

Descriptive name: Fresh Human Plasma

Bioplasma FDP is produced from pooled fresh human plasma of volunteer, non-remunerated blood donors. Each unit of plasma has been individually tested and found non-reactive for hepatitis B surface antigen (HBsAg), antibodies to the hepatitis C virus (HCV) and antibodies to the human immunodeficiency viruses, HIV-1 and HIV-2, using approved methods.

Bioplasma FDP is prepared using a solvent/detergent treatment process, which inactivates lipoprotein-coated viruses including HIV, hepatitis B and hepatitis C. This process may be of limited value against non-enveloped viruses such as hepatitis A (HAV) and parvovirus B19. To further reduce the risk of viral transmission, only plasma pools tested and found negative for anti-HIV-1 & -2, HBsAg and anti-HCV by serological testing; and for HIV, HBV, HCV and HAV by Nucleic Acid Amplification Techniques (NAT), are used in the manufacture of **Bioplasma FDP.** In addition, only pools containing <10 4 IU/ml parvovirus B19 are used.

After reconstitution with Water for injection, each 100 ml **Bioplasma FDP** contains 4 - 6 g plasma proteins with a normal distribution of human plasma components including albumin, immunoglobulins, coagulation and complement factors and their inhibitors. **Bioplasma FDP** contains a minimum of 0,4 IU/ml of each coagulation factor (II, V, VIII, IX and XI).

Bioplasma FDP contains no antimicrobial agent or preservative.

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PHARMACOLOGICAL CLASSIFICATION

A 30.3 Biologicals (Blood fractions)

PHARMACOLOGICAL ACTION

Plasma and coagulation factor replacement.

INDICATIONS

Bioplasma FDP can be used where plasma and/or coagulation factors are required.

CONTRA-INDICATIONS

Known hypersensitivity to plasma proteins, including patients with IgA deficiency. The risk of hypersensitive reactions should be weighed against that of the condition.

Severe Protein S deficiency

WARNINGS AND SPECIAL PRECAUTIONS

High infusion rates may cause cardiovascular effects as a result of citrate toxicity (fall in calcium) especially in patients with liver function disorders.

(Refer to infusion rate under **DOSAGE AND DIRECTIONS FOR USE**)

Special precautions

Adrenaline, corticosteroids and full resuscitation equipment should be on hand when administering this product. Less severe allergic reactions may be controlled with antihistamines.

Bioplasma FDP should be given with caution to a patient with diminished cardiac reserve because of circulatory overload and pulmonary oedema.

Bioplasma FDP should not be used as a volume expander where no coagulation deficiency has been documented or in coagulation factor deficiencies where the required specific factor concentrate is available for use.

The risk of parvovirus B19 infection following administration of **Bioplasma FDP** cannot be totally excluded. Parvovirus B19 infection may be serious for pregnant woman (foetal infection) (see "**PREGNANCY AND LACTATION**"), individuals with immunodeficiency or increased erythropoeisis (e.g. haemolytic anaemia), therefore **Bioplasma FDP** should only be administered to these patients after careful risk-benefit analysis.(Refer "**COMPOSITION**").

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. Consideration should be given to appropriate vaccination of patients receiving human blood or plasma-derived medicinal products on a routine basis.

It is strongly recommended that every time **Bioplasma FDP** is administered to a patient, the name and batch number of the product are recorded by the healthcare professional in order to maintain a link between the patient and the batch of the product.

Effects on ability to drive and use machines

There are no indications that Bioplasma FDP may impair the ability to drive or to operate machines.

INTERACTIONS

Bioplasma FDP must not be mixed or used concomitantly with other medications as inactivation or precipitation may occur.

Solutions containing calcium should not be administered through the same intravenous line because of possible clot formation.

PREGNANCY AND LACTATION

The safety of **Bioplasma FDP** in pregnancy and lactation has not been established in controlled clinical trials. However, **Bioplasma FDP** is a normal constituent of human blood, and therefore may be used if clearly needed during pregnancy after careful risk-benefit analysis. (Refer to "**WARNINGS AND SPECIAL PRECAUTIONS**.")

DOSAGE AND DIRECTIONS FOR USE

Dosage and infusion rate are based on the clinical picture and the results of coagulation tests. Coagulation factor levels should be maintained above 30 % of normal values. A starting dose of 12 - 15 ml/kg is generally adequate. A sufficient volume should be administered to stop bleeding and maintain haemostasis.

In massive transfusion, infusion of one plasma unit after every three units of packed cells is advised. It is important to monitor the response, both clinically and with measurement of prothrombin time (PT), partial thromboplastin time (PTT) or specific factor assays. The volume and frequency of plasma exchange varies depending on the individual patient, the clinical situation and the preferred regimen of treatment. The volume of the plasma exchanged in most therapeutic procedures is usually equivalent to the plasma volume of the patient. As a guideline, a course of 4 - 5 plasma exchange procedures within 7 - 10 days is generally followed.

Reconstitution procedure and directions for use:

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Read all instructions before commencing the reconstitution procedure. Please note that there are separate reconstitution procedures for Bioplasma FDP 200 ml and Bioplasma FDP 50 ml presentations. Bioplasma FDP 50 ml must be reconstituted using 50 ml Water for injection only.

Remove the aluminium closures from the **Bioplasma FDP** and diluent (Water for injection).

Swab the exposed rubber stoppers with a suitable antibacterial agent.

Reconstitution procedure –

Bioplasma FDP 200 ml:

1. Insert the airvent set needle into one side of the central port (A) of the diluent bottle to release the vacuum (Figure 1).

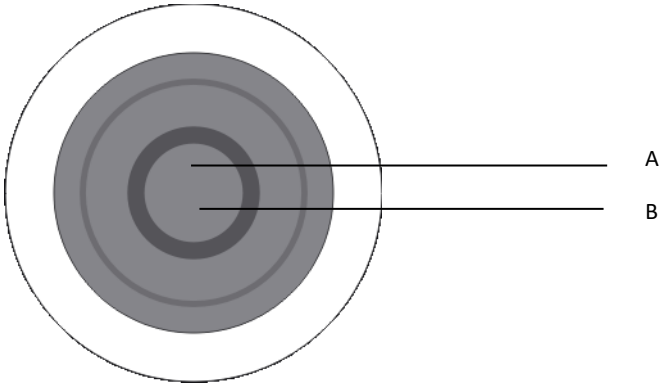


Figure 1

2. Clamp the transfer set and insert it into the other side of the central port of the diluent (B).

3. Insert the opposite end of the transfer set into the port of the **Bioplasma FDP** bottle (Figure 2).



Figure 2

4. Holding the airvent set tubing against the diluent bottle, raise the diluent bottle above the **Bioplasma FDP** bottle and release the clamp of the transfer set (Figure 3). The vacuum in the **Bioplasma FDP** will draw the diluent into the bottle.



Figure 3

5. Once the transfer is complete, remove the transfer set and the diluent bottle from the **Bioplasma FDP** bottle as a unit and discard.

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Reconstitution procedure –

Bioplasma FDP 50 ml:

1. Insert the airvent set needle into one side of the central port (A) of the diluent bottle to release the vacuum (Figure 1).

2. Connect the needle to the syringe and insert into the other side of the central port of the diluent bottle (B).

3. Draw up **50 ml** of Water for injection into the syringe. Insert this into the central port of the **Bioplasma FDP** bottle. The vacuum in the **Bioplasma FDP** will draw the diluent into the bottle. Discard the needle, syringe and the remaining diluent in the bottle.

NB: Lyophilised powders are packed under vacuum. If this vacuum is lost, it may be difficult to reconstitute this product as the diluent flow into the bottle will decrease and eventually stop. Should this occur, insert an airvent needle through the rubber stopper of the Bioplasma FDP bottle and draw the diluent into the bottle by gravity.

After transfer of the diluent, gently swirl the bottle. Do not shake and avoid foaming. Allow the product to stand until completely dissolved, swirling occasionally. This may take up to 20 minutes.

Intravenous administration:

Please note: The reconstituted solution is slightly opalescent and may exhibit slight foaming.

Do not use if preparation contains particles or is turbid.

Administer only once all the powder has completely dissolved.

Infuse immediately after reconstitution.

Insert the airvent set approximately 2 mm from the port of the rubber stopper to break the vacuum. Infuse the solution through an appropriate administration set with an in-line filter, inserted into the port of the rubber stopper, with the airvent in place to vent the infusion.

Infusion rate:

Due to the risk of citrate toxicity, the infusion rate should never exceed 0,02 - 0,025 mmol citrate/kg body mass/min equal to < 1 ml **Bioplasma FDP/**kg body mass/min.

Discard any unused portion.

SIDE EFFECTS

The following side effects may occur with **Bioplasma FDP:**

Skin and appendages disorders: Less frequent: Cutaneous manifestations (urticaria, pruritis, increased sweating)

Central & Peripheral nervous system disorders: Less frequent: Dysphonia

Psychiatric disorders: Less frequent: Agitation

Gastro-intestinal disorders: Less frequent: Vomiting, abdominal pain, nausea, diarrhoea

Metabolic and nutritional disorders: Less frequent: Citrate toxicity (Hypocalcaemia)

Cardiovascular disorders, general: Less frequent: Hypotension, cardio-respiratory collapse due to hypersensitivity to infused proteins or anti-IgA.

Heart rate and rhythm disorders: Less frequent: Tachycardia

Vascular (extracardiac) disorders: Less frequent: Flushing of the skin, vasodilation.

Respiratory system disorders: Less frequent: Pulmonary manifestation, bronchospasms, dyspnoea.

Body as a whole – general disorders: Less frequent: Chills with/without fever, back pain, substernal pain, allergic and anaphylactic reactions (due to hypersensitivity to infused proteins and IgA.)

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Hypervolaemia, pulmonary oedema and cardiac failure may occur in cases of high dosages, or infusion rates which may lead to citrate toxicity.

Treatment is symptomatic and supportive.

IDENTIFICATION

Lyophilised powder: light-yellow to yellow powder or solid friable mass.

Reconstituted solution: slightly opalescent yellow solution.

PRESENTATION

Pack sizes available:

200 ml: Lyophilised powder vacuum packed in a 250 ml clear glass bottle sealed with a rubber stopper and an aluminium closure. A 200 ml Water for injection and reconstitution kit (transfer set and 2 airvent sets) are also included.

50 ml: Lyophilised powder vacuum packed in a 100 ml clear glass bottle sealed with a rubber stopper and an aluminium closure. A 200 ml Water for injection and reconstitution kit (2 airvent sets, syringe and needle) are also included.

STORAGE INSTRUCTIONS

Store at or below 25 °C.

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Protect from light.

Keep out of reach of children.

REGISTRATION NUMBER

28/30.3/0405

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

NATIONAL BIOPRODUCTS INSTITUTE NPC

Company Reg. No. 1994/002044/08

NPO Reg. No. 020-898-NPO

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DATE OF PUBLICATION OF THE PACKAGE INSERT

Approval date: 09/01/2015

Amendment date: To be allocated.

Namibia	S2
Reg. No.: 04/30.3/1043	

Botswana	S2
Reg. No.:	BOT0200556