

Immuno Ltd

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HUMAN ALBUMIN FRACTION (SALINE) **BP 4.3% 'IMMUNO'** **HUMAN PLASMA PROTEIN FRACTION** **BP 4.3% 'IMMUNO' (PPF)**

Presentation Human Plasma Protein Fraction BP 4.3% Immuno is a clear amber liquid, presented as a solution for intravenous administration to human beings.

Human Plasma Protein Fraction BP 4.3% Immuno contains albumin and heat stable alpha- and beta- globulins prepared from human plasma. As stabilisers sodium caprylate and sodium acetyltrypophanate have been added, both at a concentration of 0.004M.

Uses Human Plasma Protein Fraction BP 4.3% Immuno is indicated for volume replacement in hypovolaemic shock (e.g. following crush injury, severe trauma, surgery, burns or abdominal emergency) and for use whenever a predominant loss of plasma fluid has occurred.

Dosage and administration Adult dosage of Human Plasma Protein Fraction BP 4.3% Immuno for hypovolaemic shock is in the range of 250–500 ml. A flow rate of up to 16 ml/min (1 litre/hr) has been well tolerated in adults. The rate of infusion, which can be increased in emergency treatment, depends on response. In hypoproteinaemia the usual dosage range is 1,000–1,600 ml daily (equivalent to 43–70 g plasma protein), but larger amounts can be given in severe hypoproteinaemia with continuing loss. The flow rate should not exceed 5–8 ml/min.

Dosage for infants and young children in whom Human Plasma Protein Fraction BP 4.3% Immuno is indicated for shock due to dehydration or infection, should be in the range of 20–30 ml/kg body weight, infused at a rate of 10 ml/min. The infusion rate should be adjusted in accordance with the clinical response. Administration is by intravenous infusion. A site should be chosen away from the area of injury or infection.

Contra-indications, warnings, etc Careful monitoring of the patient's clinical condition is necessary so that hypervolaemia is not caused. Signs to be watched for are dyspnoea, pulmonary oedema, rise of blood pressure and central venous pressure.

Careful selection of donors and the inclusion of filtration and heating at 60°C for 10 hours in the preparation of the product have virtually eliminated the risk of Serum Hepatitis. As with all blood products, however, this risk cannot be absolutely excluded.

A turbid solution must not be given. Once set up, the entire contents of the infusion bottle should be administered within four hours.

Pharmaceutical precautions Human Albumin Fraction (Saline) BP 4.3% Immuno Human Plasma Protein Fraction BP 4.3% Immuno (PPF) can be stored at +2°C to +25°C. It must be protected from light. The shelf-life is five years.

Legal category POM.

Package quantities Human Albumin Fraction (Saline) BP 4.3% Immuno Human Plasma Protein Fraction BP 4.3% Immuno (PPF) is supplied in 50 ml, 250 ml, and 400 ml infusion bottles.

Further information Human Albumin Fraction (Saline) BP 4.3% Immuno Human Plasma Protein Fraction BP 4.3% Immuno (PPF) is processed in such a way that removal of all isoagglutinins and other antibodies is achieved. It can therefore be given without restriction to patients, regardless of blood group. It will not interfere with subsequent blood investigations.

Product licence number 0215/0002.

HUMAN ALBUMIN 20% BP IMMUNO

Presentation Human Albumin 20% BP Immuno is a solution in water of human albumin containing a low proportion of salt and thus described as Salt Poor Albumin. It is a clear liquid varying in colour from amber to orange-brown and is presented as a solution for intravenous injection or infusion to human beings. It is prepared from the plasma of donors whose transaminase levels are constantly checked and whose donations are shown by RIA to be free from HBsAg. It contains 20% of protein of which at least 97% is albumin, the rest being thermostable alpha and beta globulins.

It is stabilised with 0.02 molar Sodium Caprylate and 0.02 molar Sodium Acetyldityryptophanate.

There is no preservative added to the solution.

Uses For treating Hypoalbuminaemia, Oedema, Hyperbilirubinaemia, Eclampsia, Septic Shock and Shock due to endotoxins, Human Albumin 20% BP Immuno is administered as an injection or an infusion.

For the treatment of the acute phase of Burns or Haemorrhagic Shock Human Albumin 20% BP Immuno is diluted with three parts of dextrose, laevulose or electrolyte solutions and the resulting 5% solution administered by infusion.

Dosage and administration *Hypoalbuminaemia and oedema:* Adults 100–400 ml Human Albumin 20% BP Immuno given slowly daily. Children and infants 1.5–6 ml Human Albumin 20% BP Immuno per kg body weight given slowly daily. In oedema Human Albumin 20% BP Immuno is used in combination with diuretics.

Hyperbilirubinaemia: 5–10 ml Human Albumin 20% BP Immuno can be injected or transfused into the newly born or added to a blood transfusion if exchange is being carried out.

Eclampsia: Fluid balance disturbance during pregnancy, together with increased vascular permeability, may lead to pre-eclamptic symptoms. Restoration of the circulatory disorder to normal with Human Albumin 20% BP Immuno effectively lessens the danger of eclampsia. Recommended dosage: 50 ml Human Albumin 20% BP Immuno (10 g) daily.

Septic shock and shock due to endotoxins: Cases of shock with a high packed cell volume resulting from

Hypovolaemia due to loss of fluid into the extravascular compartments should be treated with Human Albumin 20% BP Immuno to ensure the return of fluid into the circulation.

Dosage: Adults 50–200 ml Human Albumin 20% BP Immuno. Children 1–2 ml Human Albumin 20% BP Immuno. The initial dose should be infused over a period of 5–15 minutes.

Burns: In the acute phase of extensive and severe burns Human Albumin 20% BP Immuno is diluted with dextrose laevulose or electrolyte solutions to provide a 5% solution.

Dosage: Adults 800–1,600 ml Human Albumin 5%. Children 16 ml Human Albumin 5%. The total dosage over the first 24 hours should be in accordance with the formula 2 ml times body weight in kg times percentage of surface burned plus 1,500 ml. Any resulting Hypoproteinaemia can be corrected by the following dosage. Adults 50 ml Human Albumin 20% BP Immuno twice daily. Children 1 ml Human Albumin 20% BP Immuno per kg body weight twice daily.

Haemorrhagic shock: Shock due to blood loss should be treated with blood, if available, or with Human Albumin 20% BP Immuno diluted to 5%.

Dosage: Adults 200–800 ml Human Albumin 5%. Children 4–8 ml Human Albumin 5% per kg of body weight. An initial dose of 400 ml of 5% solution should be infused rapidly and repeated if shock is not controlled.

Contra-indications, warnings, etc Human Albumin 20% BP Immuno must only be used if the solution is clear. Once the cap has been pierced by a needle, the contents must be used within four hours.

Caution is indicated in the administration of Human Albumin 20% BP Immuno to patients suffering from hypertension or in cases of latent or manifest cardiac insufficiency. The single doses should be reduced to relatively small amounts and the infusion given slowly. A careful watch must be kept for the possible development of pulmonary oedema. If pulmonary oedema occurs the infusion should be stopped immediately.

In all cases of considerable blood loss, whole blood or erythrocyte concentrate must be given in addition to Human Albumin 20% BP Immuno. Careful selection and testing of donors and donations and the inclusion of filtration and heating at 60°C for 10 hours in the preparation of the product have virtually eliminated the risk of Serum Hepatitis. As with all blood products, however, this risk cannot be absolutely excluded. Intolerance reactions are extremely rare with Human Albumin 20% BP Immuno.

Pharmaceutical precautions Human Albumin 20% BP Immuno should be stored between +2°C and +25°C. It must be protected from the light. The shelf life is three years.

Legal category POM.

Package quantities Human Albumin 20% BP Immuno is supplied in rubber capped vials of 10 ml, 50 ml and 100 ml.

Further information Human Albumin 20% BP Immuno is processed in such a way that removal of all antibodies, particularly isoagglutinins, is achieved. It can therefore be given to patients regardless of their blood group or rhesus factor. It will not interfere with subsequent blood investigations.

Product licence number 0215/0009.

PROTHROMPLEX*

Presentation Prothromplex is a white, amorphous freeze-dried powder or friable solid without any

characteristic odour. It is packed in rubber-capped vials containing 200 units or 500 units each of Factors II, IX and X.

It is prepared from the plasma of donors whose transaminase levels are constantly checked and whose donations are free from HB_sAg. Pooled plasma and the final product are also tested for freedom from HB_sAg. Prothromplex is also tested to discount the likelihood of provoking disseminated intravascular coagulation.

Uses Treatment of cases of Factor IX deficiency (Haemophilia B and von Willebrand's Disease).

By administering an appropriate dose of Prothromplex, it is possible to achieve a prompt and sufficient rise of Factor IX in the patient's plasma.

The effectiveness of treatment can be checked by simple laboratory tests. The activity of Factor IX is assayed through determination of the Partial Thromboplastin Time (PTT), however the most reliable results are obtained by quantitative activity assays of Factor IX.

Dosage and administration Immediately before use Prothromplex must be dissolved in 10 ml of the solvent provided.

After sterilising the cap of the solvent bottle remove 10 ml using the disposable syringe and one of the needles provided. Next sterilise the cap of the Prothromplex bottle and introduce the solvent using the second disposable needle. Reconstitute by gently shaking to and fro, thus avoiding frothing. Withdraw the reconstituted Prothromplex, then remove the syringe from the needle and attach the third disposable needle.

Prothromplex is now ready for slow intravenous injection taking about 10 minutes.

Only general directions can be given for the dosage of Prothromplex. It is dependent upon the severity of the coagulation defect and the degree of the traumatic and haemorrhagic tissue damage. The suggested dosage for the treatment of Factor IX deficiency is given in the guide below.

Dosage guide for the treatment of severe and semi-severe cases of Factor IX deficiency: Formula for the calculation of the necessary quantity of Factor IX:

One unit of Factor IX/kg body weight = 1% increase of Factor IX in the patient's plasma.

It is suggested that a high initial dosage be chosen to ensure a rapid and sufficient increase of Factor IX thus achieving a reliable cessation of bleeding. Here, as well as with the subsequent maintenance therapy, the initially short half-life of the coagulation factors has to be considered. Depending on the *in vivo* half-life of Factor IX, which is approx. 12–30 hours, a successful result will be achieved by repeated administration of Prothromplex at intervals of 6–12 hours. To assure absolute control of treatment, determination of the PTT should be made and, where possible, quantitative assays of Factor IX activity. Treatment should be maintained up to the resorption of the tissue haemorrhage or until the wounds have healed completely, thus ensuring a complication-free post-operative course. The special advantage of Prothromplex lies in the fact that by application of small volumes of fluid and a slight amount of protein a high concentration of circulating coagulation Factor IX is achieved. The danger of volume or protein overloading of the patient is avoided even with the administration of high dosage.

Contra-indications, warnings, etc With patients suffering from disseminated intravascular coagulation, (DIC), Prothromplex should not be given unless consumption of the coagulation factors has been previously interrupted by Heparin.

Side effects are rarely observed during treatment with Prothromplex though the following reactions may occur:

1. **Allergic reactions:** All forms of allergic reactions from mild and temporary urticarial rashes to severe anaphylactic shock are possible when human plasma derivatives are administered. If these occur, treatment with Prothromplex must be interrupted at once. Allergic reactions should be controlled with antihistamines and glucocorticoids and routine shock-treatment given by anaphylactic shock. Careful and frequent recording of pulse rate and blood pressure is essential. If the pulse rate increases and/or the blood pressure falls a transfusion of 5% Dextrose should be started.

2. Despite the precautions taken in the checking of donors, donations and the final product, the transmission of hepatitis cannot be entirely excluded following the administration of coagulation factors.

3. During every type of therapy involving blood or coagulation factor concentrates, the occurrence of a circulating coagulation factor inhibitor is a possibility. The time at which such an inhibitor is produced cannot be predicted and depends neither on the amount of the plasma preparation administered nor in the frequency of administration.

As far as is known neither corticosteroids nor immunosuppressive agents significantly influence the formation of inhibitors.

Pharmaceutical precautions Prothromplex has a shelf life of one and a half years when stored between +2°C and +6°C, protected from light.

Legal category POM.

Package quantities 200 units or 500 units of Factors II, IX and X in each container.

1 rubber-capped vial containing lyophilised Prothromplex.

1 rubber-capped vial containing 10 ml Water for Injections BP.

1 10 ml disposable syringe.

3 disposable needles.

Further information Prothromplex can be stored in a domestic refrigerator, and can therefore be kept available for home treatment.

Prothromplex can be given in small volume injections, and is therefore suitable for home treatment.

Prothromplex can be moved in insulated containers to a refrigerator at some other location, giving a patient a greater degree of mobility.

Product licence numbers

200 units 0215/006

500 units 0215/007

KRYOBULIN* DRIED HUMAN ANTI-HAEMOPHILIC FRACTION BP

Presentation Dried Human Antihæmophilic Fraction is a white to yellowish amorphous powder or a friable solid without any characteristic odour.

It is prepared from the plasma of donors whose transaminase levels are constantly checked and whose donations are free from HBsAg. Pooled plasma and the final product are also tested for freedom from HBsAg.

It is packed in vials each containing approximately 250, 500 or 1,000 International Units of Factor VIII. Separate vials of solvent are also provided, these being Water for Injections BP.

One International Unit is the amount of Factor VIII activity contained in 14.365 mg of the International Standard, and is approximately equivalent to the Factor VIII activity in 1 ml of average normal plasma.

Uses Kryobulin corrects Factor VIII deficiency, and is used in the treatment of bleeding due to such deficiency in:

Haemophilia A

von Willebrand's disease

Haemophilia complicated by Factor VIII inhibitors

Thrombocytopenia with decreased Factor VIII activity

Prothromplex Dosage Table

Clinical manifestation	Therapeutically wanted minimum Factor IX level	Initial dose in units Factor IX per kg body weight	Maintenance dose at intervals of 6-12 (24) hours in units Factor IX per kg body weight
Surface bleedings of the skin and mucosae			
Superficial or deep haematoma			
Haemarthroses	5-10%	15 U	7-15 U
Slight bleedings following injuries			
Uncomplicated dental extractions			
Severe muscle haematoma			
Moderate bleedings following injuries			
Gastric and intestinal haemorrhages			
Bone fractures	15-30%	20-30 U	15-30 U
Cerebral bleedings			
Haematuria			
Complicated dental extractions			
Minor surgery			
Major surgery	more than 50%	75 U	50-75 U

Dosage and administration Frequent tests of the patient's plasma level of Factor VIII must be made to allow correction of deficiency by Kryobulin administration, but for guidance an estimation of the required dosage can be made by the following calculation:

To achieve an increase of Factor VIII concentration of 1% it is necessary to administer 1 i.u. of Kryobulin per kg body weight, both for adults and children.

Initial treatment requires doses to be given at shorter intervals than in maintenance therapy, to provide an initial high level of activity and to replenish the extravascular compartment.

Bleeding from skin, nose and oral mucous membrane: Initial dose should be 10 i.u./kg at intervals of 6–12 hours.

Haemarthrosis: Initial dose should be approximately 10 i.u./kg and the maintenance dose 5–10 i.u. per kg at intervals of 6–12 hours. Combined with immobilisation of the affected joint for several days, the treatment should be sufficient to restore function.

Bruising: In most cases a single dose of 10 i.u./kg is sufficient. For widespread bruising, repeated administration of 5–10 i.u./kg at intervals of 6–12 hours may be required.

Heavy bleeding into muscles: Immediate treatment is required to prevent permanent deformity and loss of function, and initial immobilisation of the affected area is important. An initial dose of 15–20 i.u./kg should be given, the maintenance dose to be 10 i.u./kg at intervals of six hours from the first to the second day, and at intervals of 12 hours from the third to the fifth day.

Haematuria: Initial dose should be 15–20 i.u./kg, the maintenance dose to be 10 i.u./kg at intervals of 12 hours.

Major surgery on haemophilic patients: Initial dose should be at least 25–50 i.u./kg, the maintenance dose to be 20–40 i.u./kg at intervals of four hours from the first to the fourth day, of eight hours from the fifth to the eighth day, and of 12 hours until all wounds are healed.

The effect of treatment must be checked daily. Factor VIII activity should not be allowed to fall below 50% of normal average values. It is important that treatment be continued until all wounds have healed completely, as the risk of haemorrhage persists till then.

In addition to monitoring Factor VIII activity, tests for the development of Factor VIII inhibitors should also be made.

Dental extractions: Dosage required depends on the number and type of teeth to be extracted, and on the severity of the haemophilia. If *one or two* teeth are in be extracted from a patient with severe haemophilia an initial dose of 10–20 i.u./kg should be given initially. Maintenance treatment with this dosage at intervals of six hours from the first to the third day, and eight hours from the fourth to the eighth day after extraction, should be given. If *more than two teeth* are to be extracted from patients with severe haemophilia a minimum initial dose of 20–30 i.u./kg should be given, the maintenance dose to be 10–20 i.u./kg at intervals of six hours from the first to the third day, and of eight hours for 12 more days. The plasma concentration of Factor VIII should not be allowed to fall below 10% of the normal average.

Factor VIII assay should be used to monitor the effectiveness of treatment, as partial thromboplastin time gives a less accurate value when large quantities of Kryobulin are being used.

Kryobulin must be administered intravenously, at a rate not exceeding 10 ml in three minutes.

Contra-indications, warnings, etc Although the danger of volume overload is small with Kryobulin during major surgery, monitoring of the patient's central venous pressure and blood pressure, and serial chest X-rays, may be advisable.

In disseminated intravascular coagulation associated with low Factor VIII levels Heparin should be given to interrupt intravascular coagulation before therapy with Kryobulin is started.

A low incidence of adverse reactions is experienced with Kryobulin, but the following may occur:

1. Allergic reactions: All forms of allergic reaction from mild and transient urticaria to severe anaphylactic shock are possible when human plasma derivatives are administered. If such reactions occur, treatment with Kryobulin must be interrupted at once. Allergic reactions should be controlled with antihistamines and corticosteroids and routine treatment given for anaphylactic shock. Monitoring of pulse rate and blood pressure is essential. If the pulse rate increases and/or blood pressure falls transfusion of 5% Dextrose should be started.

2. Hepatitis: Despite the precautions taken in the selection and testing of donors and donations, the risk of transmitting hepatitis cannot be entirely excluded.

3. Factor VIII Inhibitors: The appearance of a circulating Factor VIII inhibitor is possible. Its appearance cannot be predicted as it does not relate to the amount of Kryobulin administered, nor to the frequency of administration. As far as is known neither corticosteroids nor immunosuppressive agents significantly influence the formation of inhibitors.

Pharmaceutical precautions Kryobulin must be stored between 2° and 6°C, and protected from light. It then has a shelf-life of one and a half years.

Legal category POM.

Package quantities Packs of Kryobulin injection contain:

1 rubber-capped vial containing 250, 500 or 1,000 i.u. Dried Human Antihæmophilic Fraction BP.

1 rubber-capped vial containing Water for Injections BP.

Home Treatment Packs (250 and 500 i.u.) also contain:

Syringe(s), i/v needles, winged adaptor needle and filter.

Hospital Packs (500 and 1,000 i.u. contain:

Filter needle and venting needle.

Further information Kryobulin can be stored in a domestic refrigerator, and can therefore be kept available for home treatment.

Kryobulin can be given in small volume injections, and is therefore suitable for home use.

Kryobulin can be moved in insulated containers to a refrigerator at some other location giving a patient a greater degree of mobility.

Product licence number 0215/0003.

* Trade Mark