MODULE 1.3 SOUTH AFRICAN LABELLING AND PACKAGING

1.3.1 South African Package Insert

1.3.1.1 Proposed Package Insert

SCHEDULING STATUS S4

PROPRIETARY NAME (AND DOSAGE FORM)

Albusol ® 20 % (Solution for IV Infusion)

COMPOSITION

Descriptive name: Human Plasma Albumin 20 %

Albusol 20 % is prepared from pooled 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, antibodies to the hepatitis C virus and for antibodies to the human immunodeficiency viruses, HIV-1 and HIV-2, using approved methods.

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, testing of plasma pools by NAT (Nucleic Acid Amplification Techniques) for HCV and HIV RNA, and the inclusion of effective manufacturing steps for the inactivation / removal of viruses.

Albusol 20 % solution is prepared by cold ethanol fractionation to further reduce the risk of viral transmission.

Albusol 20 % solution is sterilised by filtration and then pasteurised by heating for 10 hours at 60 °C, a process that has been validated and shown to be effective against HIV, HCV and HBV 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.

Albusol 20 % is a sterile solution containing 20 % *m/v* (10 g/50 ml, 20 g/100 ml) human plasma albumin. It is stabilised with 16 mmol/l sodium acetyltryptophanate and 16 mmol/l sodium caprylate.

The solution is at pH 7. Each litre of solution contains less than 100 mmol sodium ions, less than 10

mmol potassium ions and less than 20 mmol citrate ions.

Albusol 20 % contains no antimicrobial agent or preservative.

PHARMACOLOGICAL CLASSIFICATION

A 30.3 Biologicals (Blood Fractions).

PHARMACOLOGICAL ACTION

Albumin is the dynamic protein in plasma responsible for maintaining the plasma colloid osmotic pressure thereby regulating intravascular blood volume. It also has a transport function and is a carrier of hormones, enzymes, medicinal products and toxins.

The oncotic effect of human albumin 20% is approximately four times that of blood plasma.

Less than 10% of infused albumin leaves the intravascular compartment during the first 2 hours following infusion. As a result the circulating volume will increase from 1 to 3 hours after administration.

INDICATIONS

Albusol 20 % is indicated in the following instances

- Hypovolaemic shock: **Albusol 20 %** is indicated in the treatment of hypovolaemic shock associated with blood loss, trauma and surgical procedures. Albumin solutions are an accepted form of resuscitation, although crystalloids are the initial fluid of choice

- Burns: Use for severe burns (> 15 % body surface area) after the first 24 hours if hypoproteinaemia develops and/or to maintain plasma volume.

- Hypoproteinemia: **Albusol 20 %** is indicated in the treatment of hypoproteinaemia caused by a loss of plasma proteins. Loss of plasma proteins may occur through decreased absorption in gastrointestinal disorders, inadequate synthesis in chronic liver disease or excessive urinary catabolism in chronic renal disease. This loss of proteins leads to oedema, secondary to a fluid shift from the intravascular space to the interstitium and a compensatory increase in salt and

water retention. Albumin serves to restore colloid osmotic pressure and in, conjunction with a diuretic, promotes diuresis.

- Ascites: **Albusol 20 %** may be used to maintain cardiovascular function following removal of large volumes of ascitic fluid.

- Plasma exchange/dialysis: **Albusol 20 %** may be used as an adjunct in patients who are undergoing long-term haemodialysis and are susceptible to shock and hypotension, or in dialysis patients who are hypovolaemic and may not tolerate large volumes of crystalloid infusion as treatment for shock or hypotension.

CONTRA-INDICATIONS

A history of allergic reaction to albumin preparations.

Infusion of albumin solutions is contra-indicated in patients in whom hypervolaemia and its consequences (e.g. increased stroke volume, elevated blood pressure) or haemodilution could represent a special risk for the patient. Examples of such conditions are:

- Decompensated cardiac insufficiency
- Hypertension
- Oesophageal varices
- Pulmonary oedema
- Haemorrhagic diathesis
- Severe anaemia
- Renal and post-renal anuria

(see "**SIDE EFFECTS**" and "**WARNINGS AND SPECIAL PRECAUTIONS**" and "**KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT**").

In burns and in severely shocked patients, administration of albumin solutions should be deferred until the phase of maximal capillary permeability to albumin molecules is over (i.e. after the first 24 hours).

Use of **Albusol 20 %** is contra-indicated in dehydrated patients unless it is supplemented by the infusion of crystalloid solutions to provide volume expansion.

WARNINGS AND SPECIAL PRECAUTIONS

In the USA, the Eosinophilia Myalgia Syndrome has been associated with the intake of L-tryptophan.

Suspicion of allergic or anaphylactic type reactions requires immediate discontinuation of the injection. In case of shock, standard medical treatment for shock should be implemented.

Special Precautions

If large volumes are to be replaced, monitoring of coagulation and haematocrit are necessary. Care must be taken to ensure adequate substitution of other blood constituents (coagulation factors, electrolytes, platelets, and red blood cells), if indicated.

The oncotic effect of human albumin 20 % is approximately four times that of blood plasma. Therefore, when concentrated albumin is administered, care must be taken to ensure adequate hydration of the patient. Patients should be monitored carefully to guard against circulatory overload and over-hydration.

If the required volume of human albumin 20 % exceeds 200 ml, appropriate additional electrolyte solutions should be administered to maintain normal fluid balance. Alternatively therapy may be continued with albumin 4 %.

Albumin solutions must not be diluted with Water for Injection as this may cause haemolysis in recipients. The manufacturers do not recommend dilution of **Albusol 20 %** due to sterility concerns as a result of the dilution process. Should a diluted albumin solution be required, it is recommended that human albumin 4 % solution be used.

It is strongly recommended that every time that you administer **Albusol 20 %** to a patient, the name and batch number of the product are recorded in order to maintain a link between the patient and the batch of the product.

Use within three hours of opening.

Do not use if turbid or if a precipitate is present

INTERACTIONS

No specific interactions of **Albusol 20 %** with other medicinal products are known.

PREGNANCY AND LACTATION

The safety of **Albusol 20 %** in human pregnancy has not been established in controlled clinical trials. However, human albumin is a normal constituent of human blood therefore **Albusol 20 %** may be used if clearly needed during pregnancy.

DOSAGE AND DIRECTIONS FOR USE

Albumin solutions need not be given through a filter. No compatibility testing (crossmatching) need be performed since no ABO blood group antibodies are present.

Albusol 20 % is hyperosmotic and should be given by slow intravenous infusion at a rate of about 1 ml per minute. The rate of infusion and the total volume of albumin administered ultimately must be guided by the haemodynamic response of the patient and the clinical indication for which it has been prescribed.

Transfusions of whole blood or packed red blood cells may be necessary following administration of large volumes of albumin to restore the haemoglobin concentration and prevent anaemia.

Dosage guidelines

The following doses are included as a guide only. The doctor should determine appropriate therapy after clinical assessment of the patient. Serum albumin values alone should not be used to determine dosage.

If human plasma albumin is to be administered, haemodynamic performance should be monitored regularly; this may include:

- arterial blood pressure and pulse rate
- central venous pressure
- pulmonary artery wedge pressure
- urine output
- electrolytes
- haemoglobin

Hypovolaemia	**Adult dosage:** Approximately 25 grams administered as an IV infusion. If adequate clinical response is not achieved within 15 to 30 minutes, an additional dose may be given. **Paediatric dosage:** Approximately 2,5 to 12,5 grams in total or 0,5 to 1 gram per kg of body mass administered as an IV infusion. If adequate clinical response is not achieved within 15 to 30 minutes, an additional dose may be given.
Burns	**Adult and paediatric dosage:** It is recommended that therapy begin with the administration of large volumes of crystalloid infusion to maintain plasma volume. After 24 hours, albumin may be added at an initial dose of 25 grams, with the dose adjusted thereafter.
Hypoproteinaemia	**Adult dosage:** 50 to 75 grams administered IV.
Ascites	Dosage as per Hypovolaemia .
Plasma exchange/dialysis	**Adult dosage:** Administer 25 grams as an IV infusion. Note: Infusion rate should not exceed 30 ml/min during plasma exchange.

SIDE EFFECTS

Gastrointestinal: Less frequent: Nausea, vomiting, increased salivation

Skin and appendages: More frequent: Urticaria

Autonomic nervous system: Less frequent: Flushing

Body as a whole/ General disorders:

More frequent: Chills, febrile reactions, fever

Rare: Acute allergic shock

Cardiovascular disorders(general):

Rare: Rapid increases in circulating volume can cause vascular overload, haemodilution and pulmonary oedema. Caution is advised in patients with low cardiac reserve or cardiac insufficiency.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Hypervolaemia may occur if the dosage and rate of infusion are too high. At the first clinical signs of cardiovascular overload (headache, dyspnoea, jugular vein congestion) or increased blood pressure, raised central venous pressure and pulmonary oedema, the infusion must be stopped immediately. Additionally, diuresis or cardiac output should be increased according to the severity of the clinical condition.

IDENTIFICATION

A clear, moderately viscous, amber solution.

PRESENTATION

Pack sizes available

100 ml: Albusol 20 % in a clear glass bottle with a rubber stopper and an aluminium closure.

50 ml: Albusol 20 % in a clear glass bottle with a rubber stopper and an aluminium closure.

STORAGE INSTRUCTIONS

Store at or below 25 °C.

Protect from light.

Keep out of reach of children.

Discard any unused material.

REGISTRATION NUMBER

T/30.3/739

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

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NPO Reg. No. 020-898-NPO

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NAMIBIA	S2
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