SCHEDULING STATUS **S4**

1 NAME OF THE MEDICINE

Albusol® 4 %, 0,04 g/ml, solution for infusion.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Albusol 4 % is a sterile solution containing 0,04 g/ml of total protein of which at least 95 % is human albumin.

A bottle of 200 ml contains 8 g of human albumin.

A bottle of 400 ml contains 16 g of human albumin.

Albusol 4 % is mildly hypo-oncotic to normal plasma.

Albusol 4 % is produced from pooled human plasma of healthy 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 for antibodies to the human immunodeficiency viruses, HIV-1 and HIV-2, using approved methods.

Additionally, testing of plasma pools is done by Nucleic Acid Amplification Technique (NAT) for HCV and HIV, hepatitis A virus (HAV) and hepatitis B virus (HBV).

To limit the potential burden of Parvovirus B19, the plasma pools are tested for Parvovirus B19 using validated NAT tests.

Albusol 4 % solution is prepared by cold ethanol fractionation to further reduce the risk of viral transmission.

Albusol 4 % 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.

Excipients with known effect:

Sodium (≤ 160 mmol/l).

Albusol 4 % is sugar free.

For a full list of excipients, see section 6.1.

Albusol 4 % does not contain any antimicrobial preservative.

3 PHARMACEUTICAL FORM

Solution for infusion.

The solution is a clear, slightly viscous liquid which is almost colourless to amber in colour.

The solution is at pH 7.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Albusol 4 % is indicated in the following instances:

- Hypovolaemic shock: **Albusol 4 %** is indicated in the treatment of hypovolaemic shock in adults and children, 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) in adults and children after the first 24 hours if hypoproteinaemia develops and/or to maintain plasma volume.
- Hypoproteinaemia: **Albusol 4 %** is indicated in the treatment of hypoproteinaemia in adults 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 4 %** may be used in adults and children to maintain cardiovascular function following removal of large volumes of ascitic fluid.

4.2 Posology and method of administration

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

The dosage and the infusion-rate should be adjusted to the patient’s individual requirements.

Posology

The dose required depends on the size of the patient, the severity of trauma or illness and on continuing fluid and protein losses. Measures of adequacy of circulating volume and not plasma albumin levels should be used to determine the dose required.

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
- haematocrit / haemoglobin

The following doses are included as a guide only:

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.

Method of administration

Human albumin can be directly administered by the intravenous route, at an infusion rate of about 1 ml per minute. The infusion rate should be adjusted according to the individual circumstances and the indication.

4.3 Contraindications

Hypersensitivity to the active substance (human albumin) or to any of the excipients or residues from the manufacturing process. (See sections 4.4 and 6.1).

4.4 Special warnings and precautions for use

Hypersensitivity

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

Hypervolaemia and/or haemodilution

Albumin should be used with caution in conditions where hypervolaemia and its consequences 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 sections 4.8 and 4.9).

Electrolyte balance

When albumin is given, the electrolyte status of the patient should be monitored (see section 4.2) and appropriate steps taken to restore or maintain the electrolyte balance.

Albumin solutions must not be diluted with water for injections as this may cause haemolysis in recipients.

Replacement of large volumes

If comparatively large volumes are to be replaced, controls of coagulation and haematocrit are necessary. Care must be taken to ensure adequate substitution of other blood constituents (coagulation factors, electrolytes, platelets, and erythrocytes).

Cardiovascular overload

Hypervolaemia may occur if the dosage and rate of infusion are not adjusted to the patient's circulatory situation. At the first clinical signs of cardiovascular overload (headache, dyspnoea, jugular vein congestion), or increased blood pressure, raised venous pressure and pulmonary oedema, the infusion is to be stopped immediately.

Transmissible agents

Standard measures to prevent infections resulting from the use of medicines 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 medicines 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.

There are no reports of virus transmissions with albumin manufactured to European Pharmacopoeia specifications by established processes.

Traceability

It is strongly recommended that every time that **Albusol 4 %** is administered 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.

L-Tryptophan

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

Sodium content

This medicine contains a maximum of 0,74 g (200 ml bottle) or 1,48 g (400 ml bottle) sodium per bottle, equivalent to 37 % and 74 % respectively of the WHO recommended maximum daily intake of 2 g sodium for an adult.

4.5 Interaction with other medicines and other forms of interactions

No interaction studies have been performed nor any interactions identified between **Albusol 4 %** and other medicines.

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of **Albusol 4 %** for use in pregnancy has not been established in controlled clinical trials. However, clinical experience with human albumin suggests that no harmful effects on the course of pregnancy, or on the foetus and the neonate are to be expected.

No animal reproduction studies have been conducted with **Albusol 4 %.**

However, human albumin is a normal constituent of human blood.

Breastfeeding

The safety of this preparation in lactation has not been established.

Fertility

There is no fertility data available.

4.7 Effects on ability to drive and use machines

No effects on ability to drive and use machines have been observed.

4.8 Undesirable effects

List of adverse reactions

Gastrointestinal disorders: Less frequent: Nausea, vomiting, increased salivation.

Skin and subcutaneous tissue disorders: More frequent: Urticaria.

Nervous system disorders: Less frequent: Flushing.

General disorders and administration site conditions: More frequent: Chills, febrile reactions, fever.

Rare: Acute allergic shock.

Cardiovascular disorders: 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.

Transmissible agents

For safety information with respect to transmissible agents, see section 4.4.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (https://primaryreporting.who-umc.org/ZA) found on SAHPRA website or to National Bioproducts Institute NPC via the email address Pharmacovigilance@nbisa.org.za.

4.9 Overdose

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 and the patient’s haemodynamic parameters carefully monitored.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: blood substitutes and plasma protein fractions, ATC code: B05AA01.

Category and class: A. 30.3. Biologicals (Blood fractions).

Human albumin accounts quantitatively for more than half of the total protein in the plasma and represents about 10 % of the protein synthesis activity of the liver.

Physico-chemical data: human albumin solution 0,04 g/ml is mildly hypo-oncotic to normal plasma.

The most important physiological functions of human albumin result from its contribution to oncotic pressure of the blood and transport function. Albumin stabilises circulating blood volume and is a carrier of hormones, enzymes, medicinal products and toxins.

5.2 Pharmacokinetic properties

Under normal conditions, the total exchangeable albumin pool is 4-5 g/kg body weight, of which 40 - 45 % is present intravascularly and 55 - 60 % in the extravascular space. Increased capillary permeability will alter albumin kinetics and abnormal distribution may occur in conditions such as severe burns or septic shock.

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).

Under normal conditions, the average half-life of albumin is about 19 days. The balance between synthesis and breakdown is normally achieved by feedback regulation. Elimination is predominantly intracellular and due to lysosome proteases.

In healthy subjects, less than 10 % of infused albumin leaves the intravascular compartment during the first 2 hours following infusion. There is considerable individual variation in the effect on plasma volume. In some patients the plasma volume can remain increased for some hours. However, in critically ill patients, albumin can leak out of the vascular space in substantial amounts at an unpredictable rate.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Caprylic acid

N-Acetyltryptophan

Sodium chloride

Hydrochloric acid (for pH adjustment)

Sodium hydroxide (for pH adjustment and dilution)

Water for injections

Electrolytes:

Sodium (≤ 160 mmol/l)

6.2 Incompatibilities

In the absence of compatibility studies, this medicine must not be mixed with other medicines, whole blood and packed red cells.

6.3 Shelf life

12 months.

From a microbiological point of view, the product should be used immediately after opening. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

6.4 Special precautions for storage

Store at or below 25 ˚C.

Do not freeze.

Store upright.

Keep the bottle in the outer carton until required for use.

Protect from light.

For in-use storage conditions, see section 6.3.

6.5 Nature and contents of container

200 ml: Albusol 4 % solution is packed in a Type II, clear, glass bottle, sealed with a bromobutyl rubber closure and an aluminium tear-off cap.

400 ml: Albusol 4 % solution is packed in a Type II, clear, glass bottle, sealed with a bromobutyl rubber closure and an aluminium tear-off cap.

Each pack consists of a bottle of **Albusol 4 %** and an airvent set.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The solution can be directly administered by the intravenous route.

Albumin solutions must not be diluted with water for injections as this may cause haemolysis in recipients.

If large volumes are administered, the product should be warmed to room or body temperature before use.

Do not use solutions which are cloudy or have deposits. This may indicate that the protein is unstable or that the solution has become contaminated.

Once the container has been opened the contents should be used immediately. Any unused product should be disposed of in accordance with local requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

NATIONAL BIOPRODUCTS INSTITUTE NPC

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8 REGISTRATION NUMBERS

T/30.3/738

Namibia	S2
Reg. No.:	04/30.3/1044

Botswana	S2
Reg. No.:	BOT0901506

9 DATE OF FIRST AUTHORISATION / RENEWAL OF AUTHORISATION

Registration date: 27 July 1993

10 DATE OF REVISION OF THE TEXT

18 December 2023