GPS Limited			Tel: 020 8863 9700	Job No: 17167	Text Sizes: Main Body Text 7pt Line Spacing 7.7pt	Fonts used: Helvetica Neue Regular
Project Name:	Zenalb 4.5 PIL Israel ADIS3SPC					
Contact:	Laura Ambrose		Client Order No.	P32318		
Date:	06/01/2017		Proof No.	1		
Operator:	Hema Joshi		Doc. Size:	150 x 260mm		

Colours: Black Pantone 5845

SUMMARY OF PRODUCT CHARACTERISTICS

ZENALB® 4.5
Human Albumin Solution

1. NAME OF THE MEDICINAL PRODUCT:
Zenalb® 4.5, a 45 g/L of human albumin solution for infusion (4.5% Solution).

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:
Zenalb® 4.5 contains 45 g/L and is a solution containing 45 g/L (4.5%) of total protein of which at least 95% is human albumin.

A vial of 100 mL contains 4.5 g of human albumin.

Zenalb® 4.5 has a mildly hypooncotic effect.

For excipients see section 6.1.

3. PHARMACEUTICAL FORM:
Solution for infusion.

A clear, slightly viscous liquid, it is almost colourless, yellow, amber or green.

4. CLINICAL PARTICULARS:

4.1 Therapeutic indications
Restoration and maintenance of circulating blood volume where volume deficiency has been demonstrated and use of a colloid is appropriate.

The choice of albumin rather than artificial colloid will depend on the clinical situation of the patient, based on official recommendations.

4.2 Posology and method of administration
The concentration of the albumin preparation, 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 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
- electrolyte
- haematocrit/haemoglobin

Method of administration
Human albumin can be directly administered by the intravenous route.
The infusion rate should be adjusted according to the individual circumstances and the indication.

In plasma exchange the infusion should be adjusted to the rate of removal.

4.3 Contraindications
Hypersensitivity to albumin preparations or to any of the excipients.

4.4 Special warnings and special precautions for use
Suspicion of allergic or anaphylactic-type reactions requires immediate discontinuation of the injection. In the case of shock, the standard medical treatment for shock should be implemented.

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

200 g/L Human albumin solutions are relatively low in electrolytes compared to 45 g/L human albumin solutions. 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.

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).

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.

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.

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

Appropriate vaccination (hepatitis A and B) should be considered for patients in regular/repeated receipt of plasma-derived human albumin solutions.

It is strongly recommended that every time that Zenalb® 4.5 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 product.

4.5 Interactions with other medicinal products and other forms of interactions
No specific interactions of human albumin with other medicinal products are known.

4.6 Pregnancy and lactation
The safety of Zenalb® 4.5 for use in human pregnancy has not been established in controlled clinical trials. However, clinical experience with albumin suggests that no harmful effects on the course of pregnancy, or on the foetus or the neonate are to be expected.

No animal reproduction studies have been conducted with Zenalb® 4.5.

Experimental animal studies are insufficient to assess the safety with respect to reproduction, development of the embryo or foetus, the course of gestation and peri and postnatal development. However, human albumin is a normal constituent of human blood.

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

4.8 Undesirable effects
Mild reactions such as flush, urticaria, fever and nausea occur rarely. These reactions normally disappear rapidly when the infusion rate is slowed down or the infusion is stopped. Very rarely, severe reactions such as shock may occur. In these cases, the infusion should be stopped and appropriate treatment should be initiated.

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Post-marketing experience:
Additional side effects reported spontaneously include rigors, hypertension, hypotension, feeling cold, tachycardia, tremor, bronchospasm, dyspnoea, chest tightness, stridor and dizziness.

For safety with respect to transmissible agents, see 4.4.

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form:

http://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

Additionally, you should also report to Kamada LTD to email address: pharmacovigilance@kamada.com

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 should be stopped immediately and the patient's haemodynamic parameters carefully monitored.

5. PHARMACOLOGICAL PROPERTIES:

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: plasma substitutes and plasma protein fractions, ATC code: B05AA01

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.

Physicochemical data: Zenalb® 4.5, human albumin 45 g/L, is mildly hypooncotic to normal plasma.

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

5.2 Pharmacokinetic properties
Under normal conditions the total exchangeable albumin pool is 4-5 g/kg bodyweight, 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.

Under normal conditions the 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 people, 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.

5.3 Preclinical safety data
Human albumin is a normal constituent of plasma and acts like physiological albumin.

In animals, single dose toxicity testing is of little relevance and does not permit the estimation of toxic or lethal doses or of a dose-effect relationship. Repeated dose toxicity testing is impracticable due to the development of antibodies to heterologous protein in animal models.

To date, human albumin has not been reported to be associated with embryo-foetal toxicity, oncogenic or mutagenic potential.

No signs of acute toxicity have been described in animal models.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of excipients
Sodium 100-160 mmol/L
Potassium
Chloride
Citrate
Sodium n-octanoate
Zenalb® 4.5 contains not more than 200 µg/L of aluminium.

6.2 Incompatibilities
Human albumin should not be mixed with other medicinal products (except those mentioned in 6.6), whole blood and packed red cells.

6.3 Shelf-life
50 mL, 100 mL, 250 mL, 500 mL
Unopened 36 months
Opened 3 hours

6.4 Special precautions for storage
Zenalb® 4.5 should be stored between 2°C and 25°C. DO NOT FREEZE. The expiry date of the product is stated on the label.

Store in the original container. Keep container in the outer carton in order to protect from light.

6.5 Nature and contents of container
The solution is contained in glass bottles stoppered with a rubber bung. The bung is over-sealed with a tamper evident cap.

6.6 Instructions for use and handling and disposal
The solution can be directly administered by intravenous route. Albumin solution 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 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 infusion container has been opened, the contents should be used immediately. Any unused product should be disposed of in accordance with local requirements.

7. MANUFACTURER:
Bio Products Laboratory Limited (BPL)
Elstree
WD6 3BX
United Kingdom.

8. LICENSE HOLDER:
Kamada Ltd, Beit Kama, Israel.

LICENSE NUMBER:
137-73-31655-00

The format of this leaflet was determined by the Ministry of Health and its content was checked and approved in November 2016.

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