GPS Limited			Tel: 020 8863 9700	Job No: 18555	Text Sizes: Main Body Text 6pt Line Spacing 7pt	Fonts used: Helvetica Neue 55 Roman 75 Bold
Project Name:	Zenalb 20 PIL Singapore ABSG4					
Contact:	Laura Ambrose		Client Order No.	P53744		
Date:	09/04/2020		Proof No.	3		
Operator:	Hema Joshi		Doc. Size:	170 x 220mm		

Colours: Pantone Process Black

ABSG4

Package leaflet: Information for the user
Zenalb 20
HUMAN ALBUMIN 20% SOLUTION

1. NAME OF THE MEDICINAL PRODUCT
Zenalb 20
200 g/l solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Zenalb 20 is a solution containing 200 g/l (20%) of total protein of which at least 95% is human albumin.

A vial of 100 ml contains 20 g of human albumin.

Zenalb 20 has a mildly hyperoncotic effect.

Excipient with known effect:
Zenalb 20 contains approximately 50-120 mmol/l sodium.

For the full list of 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
Zenalb 20 is indicated in all patients for the restoration and maintenance of circulating blood volume where volume deficiency has been demonstrated, and use of a colloid is appropriate.

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, or it can also be diluted in an isotonic solution (e.g. 5% glucose or 0.9% sodium chloride).
The infusion rate should be adjusted according to the individual circumstances and the indication.

The recommended rate of administration for patients with normal blood volume should be 1-2ml/minute (60-120ml/hour). In patients with greatly reduced blood volume and/or shock, infusion of Zenalb 20 should not exceed 120ml/hour.

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

4.3 Contraindications
Hypersensitivity to albumin preparations or to any of the excipients listed in section 6.1.

Patients with severe anaemia and patients with cardiac failure.

4.4 Special warnings and precautions for use
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 20 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.

Suspicion of allergic or anaphylactic-type reactions requires immediate discontinuation of the infusion. In the case of shock, 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

The colloid-osmotic effect of human albumin 200 g/l 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 hyperhydration.

200-250 g/l human albumin solutions are relatively low in electrolytes compared to 40-50 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.

This medicinal product contains 115 to 276 mg sodium per 100 ml, equivalent to 5.75 to 13.8% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

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

4.6 Fertility, pregnancy and lactation
Pregnancy
The safety of Zenalb 20 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.

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.

Fertility
No animal reproduction studies have been conducted with Zenalb 20.

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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
Summary of the safety profile
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.

Tabulated list of adverse reactions
Adverse reactions reported from post-marketing use of Zenalb 20 are classified according to system organ class and frequency. Frequency groupings are defined according to the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).

MedDRA Standard System Organ Class	Not known
Nervous system disorders	Tremor
Cardiac disorders	Tachycardia Dyspnoea Dizziness
Vascular disorders	Hypertension Hypotension
Respiratory, thoracic and mediastinal disorders	Stridor Bronchospasm
General disorders and administration site conditions	Feeling cold Chest tightness Rigors

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

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: human albumin 200 g/l has a corresponding hyperoncotic effect.

The most important physiological function of albumin results 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 average 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 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.

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 evaluation 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
Chloride
Sodium-n-octanoate

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

6.3 Shelf-life
Unopened 36 months
Opened 3 hours

6.4 Special precautions for storage
Store between 2°C and 25°C.
Do not freeze.

Store in the original container. Keep container in the outer carton in order to protect from light. For storage conditions after opening the medicinal product, see section 6.3.

6.5 Nature and contents of container
The solution is contained in 50 ml and 100 ml colourless glass bottles (Type II) with stopper (halobutyl rubber), with an overseal (aluminium) and tamper-evident flip-off cap (polypropylene).

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 or it can be diluted in an isotonic solution (e.g. 5% glucose or 0.9% sodium chloride).
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.
Each container is intended for single use and once the seal is punctured, the desired dose should be administered within 3 hours. Any unused product or waste material should be disposed of in accordance with local requirements.

6.7 Manufacture
Bio Products Laboratory Limited,
Dagger Lane, Elstree, Hertfordshire, WD6 3BX
United Kingdom

7. MARKETING AUTHORISATION HOLDER AND DISTRIBUTOR
Euro Asia Medico Pte. Ltd.
6 Tagore Drive, #04-13 Tagore Building
Singapore 787 623

8. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION
9th October 1992 / 10th October 2014

9. DATE OF REVISION OF THE TEXT
March 2020

POM

JAUHI DARIPADA KANAK-KANAK

bpl
Bio Products Laboratory