PRESCRIBERS INFORMATION

1 NAME OF THE MEDICINAL PRODUCT:

UMAN ALBUMIN 200 g/l, solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

	UMAN ALBUMIN 200 g/l
Solution containing total plasma proteins to	20%
of which human albumin at least to	95%
a vial of 50 ml contains human albumin equal to	10 g
a vial of 100 ml contains human albumin equal to	20 g
The solution is	hyperoncotic

Excipient with known effect: This medicinal product contains up to 157 mg sodium per vial of 50 ml and 314 mg per vial of 100 ml.

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

For 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 individual patient, based on official recommendations.

4.2 Posology and method of administration

The concentration of the albumin preparation, dosage and infusion-rate must 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.

Paediatric population
The safety and efficacy of UMAN ALBUMIN in children, including premature infants, have not been established by controlled clinical trials and its use in paediatric population is based only on estabilished medical practice. For this reason, UMAN ALBUMIN must be used in children and premature infants only if clearly necessary.

Patients with renal impairment
UMAN ALBUMIN can be administered to dialysis patients as the aluminium content of the finished product is not more than 200 μg/l.

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

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability
In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

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.

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 is approximately four times that of plasma.
Therefore, when concentrated albumin is administered, care must be taken to assure adequate hydration of the patient. Patients should be monitored carefully to guard against circulatory overload and hyperhydration.

200 g/l human albumin solutions are relatively low in electrolytes compared to the 40-50 g/l human albumin solutions. When albumin is given, the electrolyte status of the patient must 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, control***s*** of coagulation and haematocrit are necessary. Care must be taken to ensure adequate substitution of other blood constituents (coagulation factors, electrolytes, platelets and erythrocytes).
If the haematocrit drops below 30%, packed red cells must be given in order to maintain the oxygen transport capacity of the blood.
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.

Important information about excipients of UMAN ALBUMIN
This medicinal product contains up to 157 mg sodium per vial of 50 ml and 314 mg per vial of 100 ml, equivalent to 7.85 % (for vial of 50 ml) and 15.7 % (for vial of 100 ml) of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Viral safety
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.

Paediatric population

Although no specific data are available for paediatric population, the clinical experience on the use of Human Albumin in children suggests that no differences between adults and children are to be expected, provided that a careful attention to the dosage has been observed in order to avoid circulatory overload.

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 UMAN ALBUMIN 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 and the neonate are to be expected.

In general, particular attention must be paid when a substitution of volume is effected in a pregnant patient.

Breast-feeding

Since human albumin is a normal constituent of human blood, treatment of the nursing mother with UMAN ALBUMIN is not expected to present a risk to the breast-fed newborn/infant.

Fertility

No animal reproduction studies have been conducted with UMAN ALBUMIN.
However human albumin is a normal constituent of human blood.

4.7 Effects on ability to drive and use machines

UMAN ALBUMIN has no or negligible influence on ability to drive and use machines.

4.8 Undesirable effects

Summary of 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 an appropriate treatment should be initiated.

Tabulated list of adverse reactions

The table presented below is according to the MedDRA System Organ Classification (SOC) and Preferred Term Level (PT) and it includes undesirable effects occurring with the use of human albumin solutions.

Frequencies have been evaluated 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).

There are no robust data on the frequency of undesirable effects from clinical trials.
The following data is in line with the safety profile of human albumin solutions, and confirmed by the post marketing experience; as the post marketing reporting of adverse reactions is voluntary and from a population of uncertain size, it is not possible to reliably estimate the frequency of these reactions:

MedDRA System Organ Class (SOC)	**Adverse reactions (MedDRA Preferred Term)**	**Frequency**
Vascular disorders	Hypotension	Not known
Nervous system disorder	Tremor	Not known
Respiratory, thoracic and mediastinal disorder	Dyspnea	Not known
Skin and subcutaneous tissue disorder	Erythema	Not known
	Urticaria	Not known
	Pruritus	Not known
General disorders and administration site conditions	Chills	Not known
	Pyrexia	Not known

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

Paediatric population
No specific data are available on paediatric population.

Reporting of suspected adverse reactions
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:
https://sideeffects.health.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. Additionally, diuresis or cardiac output must be increased in accordance to the severity of the clinical situation.

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 functions. Albumin stabilises circulating blood volume and is a carrier of hormones, enzymes, medicinal products and toxins.

Paediatric population

No specific studies of efficacy and safety are available on paediatric population.

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.

Under normal conditions, the average half-life of albumin is about 19 days. The balance between synthesis and breakdown is normally achieved by feed-back 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 a 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.

Paediatric population

No specific studies of efficacy and safety are available on paediatric population

5.3 Preclinical safety data

Human albumin is a normal constituent of human 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

1 litre of solution for infusion contains:

Sodium chloride	4.52 g/l
Sodium caprylate	2.660 g/l (16 mmoles/l)
N-Acetyl-DL-Tryptophan	3.940 g/l (16 mmoles/l)
Water for injections	up to 1000 ml
Total concentration of sodium	123.5 – 136.5 mmoles/l

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

6.3 Shelf life
The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage
Do not store the product above 30°C.
Keep the vial in the outer carton in order to protect from light.
Do not freeze.
The storage conditions must be strictly followed.

6.5 Nature and contents of container
A card box containing a glass vial, with pierceable rubber stopper.
50 ml type II glass vial, 100 ml type II glass vial

6.6 Special precautions for disposal and other handling
The solution 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).
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 medicinal product or waste material should be disposed of in accordance with local requirements.

7 Manufacturer:
Kedrion S.p.A., Barga, Lucca, Italy.

8 License Holder:
Kamada Ltd., Beit Kama, MP Negev 8532500

9 Registration Number:
143-85-31992-00

Revised in September 2021 according to MOHs guidelines.