IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA0521/008/001
Case No: 2063102

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

Octapharma Limited

The Zenith Building, **26 Spring Gardens**, **Manchester**, **M2 1AB**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Albuminativ 200 mg/ml, solution for infusion

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **08/05/2009** until **09/10/2009**.

Signed on behalf of the Irish Medicines Board this

_____

A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Albuminativ 200mg/ml, solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Human albumin

Solution containing 20% of protein of which at least 96% is human albumin.
Each 100ml contains at least 19.2g of human albumin.
The product is mildly hyperoncotic.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion.

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 individual 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 only 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

This product is suitable for premature infants and dialysis patients.

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 albumin preparations or to any of the excipients.

4.4 Special warnings and precautions for use

If allergic or anaphylactic-type reactions occur, the infusion should be stopped immediately and appropriate treatment instituted. In case of shock, the current medical standards for shock-treatment should be observed.

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 20% or 25% is approximately four times that of blood 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.

20-25% human albumin solutions are relatively low in electrolytes compared to the 4-5% 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.

It is strongly recommended that every time that Albuminativ 40 mg/ml 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.

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 Pregnancy and lactation

The safety of human 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.
No animal reproduction studies have been conducted with this product.
However, human albumin is a normal constituent of human blood.

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

Adverse reactions for Albuminativ 200 mg/ml are rare. These reactions normally disappear rapidly when the infusion rate is slowed down or the infusion is stopped. In case of severe reactions, the infusion should be stopped and an appropriate treatment should be initiated.

The following adverse reactions have been observed for Albuminativ 200 mg/ml during the postmarketing phase.

Very common (>1/10); common (.1/100, <1/10); uncommon (>1/1,00, <1/100); rare (>1/10,000, < 1/1000); very rare (<1/10,000)

System Organ Class	Rare	Very Rare
Cardiac disorders		tachycardia bradycardia
Gastrointestinal disorders		nausea
General disorders and administration site conditions		Pyrexia chills
Immune system disorders	anaphylactic reaction hypersensitivity	anaphylactic shock
Nervous system disorders		headache
Psychiatric disorders		confusional state
Respiratory, thoracic and mediastinal disorders		dyspnoea

Skin and subcutaneous tissue disorders		Urticaria angioneurotic oedema rash erythematosus hyperhidrosis
Vascular disorders	hypotension	hypertension flushing

For information on viral safety see 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.

Physico-chemical data human: Human albumin 4-5% is mildly hypooncotic to normal plasma. Human albumin 20 or 25 % has a corresponding hyperoncotic effect.

The most important physiological functions of 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.

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 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 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

Acetyl tryptophan (4mg/ml)
Sodium caprylate (3mg/ml)
Sodium hydroxide or hydrochloric Acid (to pH 7)
Sodium Chloride
Water for injections
Maximum aluminium content: 200 micrograms/litre
Maximum content of sodium chloride: not more than 83 mmol/l (or 1.91 mg/ml)

6.2 Incompatibilities

Albuminativ 200 mg/ml should not be mixed with other medicinal products, whole blood and packed red cells.

Albuminativ 200 mg/ml can be diluted with the following infusion:
Sodium chloride 0.9%, glucose 5% and 10%, Ringer and Ringer acetate.

6.3 Shelf Life

5 years.
Once the container has been opened the contents must be used immediately.

6.4 Special precautions for storage

Do not store above 25°C.
Albuminativ is stored at room temperature. Any unused solution must be discarded owing to the risk of bacterial contamination.

Do not use after expiry date given on the label. Do not freeze. Keep container in the outer carton in order to protect from light.

6.5 Nature and contents of container

Glass bottles, type II glass (Ph. Eur.), of 50 and 100ml, stoppered with bromobutyl stoppers and sealed with a pull-off cap.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

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.

The solution should be clear or slightly opalescent. 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 MARKETING AUTHORISATION HOLDER

Octapharma Limited
The Zenith Building
26 Spring Gardens
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United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 521/8/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10 October 1994
Date of last renewal: 10 October 2004

10 DATE OF REVISION OF THE TEXT

May 2009