IRISH MEDICINES BOARD ACTS 1995 AND 2006

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

(S.I. No.540 of 2007)

PA0521/002/001
Case No: 2045324

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

Albumin Human 50g/l Octapharma, 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 **14/07/2008**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Albumin Human 50g/l Octapharma, solution for infusion.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Human albumin from human plasma source.
Solution containing 5% of protein of which at least 96% is human albumin.
Each 100ml contains 5g human albumin.
Albumin Human 50 g/l is a mildly hypooncotic pasteurized solution.

Excipients: also includes sodium 157.5mmol/litre

For a 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 supplied in Type II (Ph. Eur.) glass infusion bottles.

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 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 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
- electrolytes
- 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.

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 the case of shock, the current medical standards for treatment of shock 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
- Oesophageal varices
- Pulmonary oedema
- Hypertension
- 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 and 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 the 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 the 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 Albumin Human 50g/l Octapharma 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 yet 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

Mild reactions such as flush, urticaria, hypotension, 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.

For safety with respect to transmissible agents, see 4.4.

4.9 Overdose

Hypervolaemia may occur if the dosage and the 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 nervous 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 fractions,

ATC code: B05 AA01

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 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, drugs, toxins etc.

5.2 Pharmacokinetic properties

Under normal situations 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 a severe burns or septic shock.

Under normal conditions the average half-life of albumin is an average of 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 the 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 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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Octanoic acid/Caprylic acid (4.2 mmol/litre) (max: 0.08 mmol/g albumin)
N-Acetyltryptophan (4.2 mmol/litre) (max: 0.08 mmol/g albumin)
Sodium chloride
Sodium hydroxide
Hydrochloric acid, concentrated
Water for injections

Maximum limit for aluminium content: 200 micrograms per litre.

Maximum sodium chloride content: 157.5 mmol/litre (corresponding to 3.6mg/ml sodium ions)

Maximum potassium ion content: 1.0 mmol/litre.

6.2 Incompatibilities

Human albumin solution should not be mixed with other medicinal products, whole blood and packed red cells.

6.3 Shelf Life

Unopened: 3 years.
Once opened: Use immediately

6.4 Special precautions for storage

Do not store above 25°C.
Do not freeze.
Store in the original container.
Keep the container in the outer carton in order to protect from light.

6.5 Nature and contents of container

Glass Type II (Ph. Eur.) infusion bottles with bromobutyl rubber stoppers Type I (Ph. Eur.)
Pack sizes:
1 infusion bottle with 100ml
1 infusion bottle with 250ml
All infusion bottles are available singly or in packs of 10.

Not all pack sizes may be marketed.

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.

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.

Do not use after expiry date given on the label.

Once the infusion container has been opened the content should be used immediately.

Any unused solution should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Octapharma Limited
6 Elm Court
Coventry
CV5 9RG
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 521/2/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 14 July 1993
Date of last renewal: 14 July 2008

10 DATE OF REVISION OF THE TEXT

July 2008