NEW ZEALAND DATA SHEET

1 PRODUCT NAME

Alburex® 20 NZ, 20% (200 g/L), solution for infusion.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Human albumin

Alburex® 20 NZ is a solution containing 200 g/L of total protein of which at least 96% is human albumin.

Alburex® 20 NZ is manufactured from human plasma donated by New Zealand's voluntary and non-remunerated donors.

Excipients with known effect:

One litre of Alburex® 20 NZ also contains 16 mmol of sodium acetyltryptophanate and 16 mmol of sodium octanoate. Sodium chloride is added to give a sodium content of 140 mmol/L.

For the full list of excipients, see section 6.1.

One litre of Alburex® 20 NZ contains a total of 32.4 g of nitrogen.

3 PHARMACEUTICAL FORM

Solution for infusion.

Alburex® 20 NZ is a clear, slightly viscous liquid; it is almost colourless, yellow, amber or green.

Alburex® 20 NZ is hyperoncotic to normal plasma. It has a nominal osmolality of 258 mOsm/kg, is isotonic and the pH is 6.7–7.3.

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.

4.2 Dose and method of administration

Dose

The concentration of the albumin preparation, dosage and the infusion rate should be adjusted to the patient's individual requirements.

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. Infusion rate and volume need to be adapted according to clinical conditions, most notably in the elderly or in the paediatric population.

Monitoring advice

If Alburex® 20 NZ 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 dosage in children and adolescents (0–18 years) should be adjusted to the patient's individual requirements.

Method of administration

Alburex® 20 NZ should be administered by the intravenous route only.

The product is ready for use and can be administered as supplied either directly or it can first be diluted to a mildly hypooncotic solution to normal plasma (4–5% albumin) prior to administration, in the proportion of 1 mL of Alburex® 20 NZ to 4 mL of suitable crystalloid solution.

Alburex® 20 NZ is packaged in a glass vial that must be vented during use.

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.

For instructions on dilution of the medicine before administration, see section 6.6.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

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 g/L 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. Alburex® 20 NZ must not be diluted with water for injections as this may cause haemolysis in recipients.

200–250 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 should be monitored and appropriate steps taken to restore or maintain the electrolyte balance.

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 infusion rate 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.

Alburex® 20 NZ contains approximately 3.2 mg sodium per mL of solution (140 mmol/L). This should be noted when the product is used in patients requiring sodium restriction.

Pathogen safety

This product is made from human plasma. Products made from human plasma may contain infectious agents such as viruses and theoretically Creutzfeldt-Jakob Disease (CJD) agents, that can cause disease. The risk that such products will transmit an infectious agent has been reduced by screening plasma donors for prior exposure to certain infectious agents and by testing for the presence of certain viral markers.

The Alburex® 20 NZ manufacturing process includes pasteurisation (60°C for 10 hours) and multiple steps involving ethanol fractionation and depth filtration in the presence of filter aids which contribute to the reduction of pathogens should they be present. The current process and procedures applied in the manufacture of this product are effective against enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV), and the non-enveloped virus, hepatitis A virus (HAV) and human parvovirus B19.

Despite these measures, such products may still potentially transmit disease. There is also the possibility that other known or unknown infectious agents may be present in such products.

Vaccination for patients in receipt of medicinal products from human plasma should be considered where appropriate.

It is strongly recommended that every time that Alburex® 20 NZ 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 medicines and other forms of interaction

No specific interactions of human albumin with other medicinal products are known.

4.6 Fertility, pregnancy and lactation

Pregnancy

Reproductive toxicity studies with Alburex® 20 NZ in animals have not been conducted.

The use of Alburex® 20 NZ in human pregnancy has not been established in controlled clinical trials; therefore, use in pregnant women only if benefits outweigh risk.

Breast-feeding

Like endogenous serum albumin, Alburex® 20 NZ may be excreted in milk. No safety information is available.

Fertility

No studies examining the effect of Alburex® 20 NZ on fertility have been conducted.

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 with human albumin solutions 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 allergic reactions such as anaphylactic shock may occur. In these cases, the infusion should be stopped immediately and an appropriate treatment should be initiated.

Tabulated list of adverse reactions

Table 1 presents the adverse reactions which have been observed with CSL Behring human albumin solutions during the post-marketing phase, according to the MedDRA System Organ Class and Preferred Term level. 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. Hence the frequency category ‘not known (cannot be estimated from the available data)’ is used.

Table 1: List of adverse reactions

MedDRA System Organ Class	Adverse Reaction	Frequency
Immune system disorders	Hypersensitivity reactions (including anaphylaxis and shock)	Not known
Gastrointestinal disorders	Nausea	Not known
Skin and subcutaneous tissue disorders	Flush, urticaria	Not known
General disorders and administration site conditions	Fever	Not known

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

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions via https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

Hypervolaemia may occur if the dosage and infusion rate 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.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Plasma expanders substitutes and plasma protein fractions.

ATC code: B05AA01

Mechanism of action

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.

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, medicinal products and toxins.

5.2 Pharmacokinetic properties

Distribution

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% is 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.

Elimination

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 human plasma and its action does not differ from that of physiological human albumin. Single dose toxicity testing in animals 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 embryofoetal toxicity, mutagenic, or carcinogenic potential. No signs of acute toxicity have been described in animal models.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium acetyltryptophanate
Sodium octanoate
Sodium chloride
Water for injections

6.2 Incompatibilities

Alburex® 20 NZ must not be mixed with any other medicinal products, including whole blood, packed red cells, or other albumins, except those mentioned in section 6.6.

6.3 Shelf life

3 years

Stability after first opening:

Use in one patient on one occasion only. Alburex® 20 NZ contains no antimicrobial preservative. It must, therefore, be used immediately after opening the vial.

6.4 Special precautions for storage

Store below 25°C (Do not freeze).

Protect from light.

For storage conditions after first opening of the medicine, see section 6.3.

6.5 Nature and contents of container

Solution in a glass vial with a synthetic elastomer stopper.

Pack sizes:

One vial of 50 mL contains 10 g of human albumin.
One vial of 100 mL contains 20 g of human albumin.

6.6 Special precautions for disposal and other handling

Alburex® 20 NZ is administered intravenously.

Alburex® 20 NZ 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 if the solution has been frozen.

Alburex® 20 NZ can be diluted to a mildly hypooncotic solution to normal plasma (4–5% albumin) prior to administration, in the proportion of 1 mL of Alburex® 20 NZ to 4 mL of suitable crystalloid solution and administered by the usual intravenous technique.

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. The vial should be returned unopened to the New Zealand Blood Service.

Once the container has been opened, the contents should be used immediately.

Any unused solution must be discarded appropriately.

7 MEDICINE SCHEDULE

General Sale Medicine

8 SPONSOR

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9 DATE OF FIRST APPROVAL

01 June 2023

10 DATE OF REVISION OF THE TEXT

01 June 2023

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SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
All	New registration