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CSL Biotherapies

Australian Red Cross BLOOD SERVICE

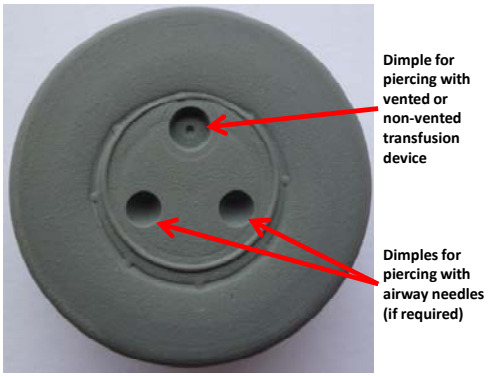
11 November 2011

Re: Redesign of ALBUMEX® and INTRAGAM® P Stoppers

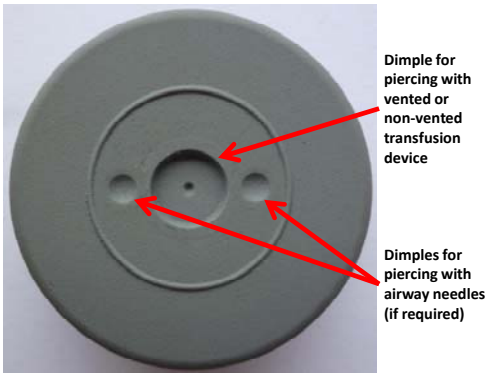
As part of CSL Biotherapies' on-going commitment to enhancing the ease of use of plasma-derived therapies fractionated under the Australian Fractionation Agreement, the stopper for ALBUMEX® (Human Albumin) and INTRAGAM® P (Human Normal Immunoglobulin) vials has been redesigned to simplify stopper piercing during preparation for infusion. There is no change to the formulation of the stopper (non-latex containing isobutyl rubber) and no effect on the shelf-life of either product.

The stopper redesign includes centralising and enlarging the dimple for piercing with the transfusion device, and relocating the dimples for piercing with airway needles. Images of the current and redesigned stopper appear below:

Current Stopper



Redesigned Stopper



Regulatory approval for the redesigned stopper has been received and CSL Biotherapies anticipates that stocks of ALBUMEX and INTRAGAM P packaged using the redesigned stopper will be supplied to you shortly.

Yours sincerely,

Dr Elizabeth Campbell
Director, Commercial Operations
Plasma-Derived Therapies
CSL Biotherapies

Dr Joanne Pink
Chief Medical Officer
Australian Red Cross Blood Service

Before prescribing, please review the Approved Product Information available on request from CSL Biotherapies

PBS Information: This product is not listed on the PBS. These products are funded under arrangements implemented by the National Blood Authority. Please refer to the National Blood Authority for details

The Medicines Australia Code of Conduct defines standards for the content of materials produced, and the conduct of promotional activities undertaken, by pharmaceutical companies within Australia. As a member of Medicines Australia, CSL Biotherapies willingly complies with the Medicines Australia Code of Conduct (www.medicinesaustralia.com.au).

Minimum Product Information Intragam® P (Human Normal Immunoglobulin 6% (6g/100mL)). Indications: IgG replacement in primary immunodeficiency disorders, myeloma and chronic lymphocytic leukaemia with severe secondary hypogammaglobulinaemia and recurrent infections, congenital or acquired immune deficiency syndrome. Immunomodulatory therapy in Idiopathic Thrombocytopenic Purpura, allogeneic bone marrow transplantation, Kawasaki disease and Guillain-Barré Syndrome. Contraindications: Patients who have had a true anaphylactic reaction to a human immunoglobulin preparation. Precautions: Intragam® P should only be administered intravenously. Intragam® P may, on rare occasions, cause a precipitous fall in blood pressure and a clinical picture of anaphylaxis. Intragam® P contains trace amounts of IgA which may provoke anaphylaxis in patients with IgA antibodies, such as those with IgA deficiency. Aseptic meningitis syndrome has been reported to occur infrequently with intravenous IgG (IVIg) treatment. Renal dysfunction, acute renal failure and thrombotic events have also been reported. Positive direct antiglobulin tests and red cell haemolysis have been reported following high dose infusions; patients with blood group A or AB appear to be more susceptible. Certain adverse events may occur more frequently with high rate of infusion, patients receiving IVIg for the first time, when there has been a long period since a previous infusion, or when the IVIg product is switched. Reactions to IVIg tend to be related to infusion rate and are most likely to occur within the first hour of infusion. Intragam® P 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, and by dedicated virus removal and inactivation procedures included in the manufacturing process. Despite these measures, such products may still potentially transmit disease. Vaccination for patients in receipt of medicinal products from human plasma should be considered where appropriate. The use of Intragam® P in pregnancy and lactation has not been established in controlled clinical trials. For all precautions and risk factors review approved PI. Interactions: Intragam® P may interfere with some blood glucose measurements and may affect the response to live, attenuated vaccines. The interaction of Intragam® P with other drugs has not been established in appropriate studies. Adverse Effects: Reported adverse events include headache, migraine, positive direct Coombs test, haemolysis, non-urticarial skin rash, nausea and vomiting. Rarely, transient haemolytic anaemia, neutropenia, acute renal failure, aseptic meningitis, hypersensitivity and thrombotic events have been reported. For all adverse events review approved PI. Dosage & Administration: For replacement therapy, patients usually require 0.2 to 0.6 g per kg body weight per month. For immunomodulatory therapy, refer to full PI. Infusion should be commenced at a rate of 1.0 mL/min. After 15 minutes increase slowly to maximum of 3-4 mL/min. If symptoms develop the infusion rate should be slowed or stopped temporarily. Contains no antimicrobial agent, use immediately after opening. Do not use if turbid. Intragam® P should be administered separately from other intravenous fluids or medications. Based on Intragam® P Approved Product Information, date of most recent amendment: 7 December 2007 (V 11/11).

Minimum Product Information: ALBUMEX® 4 (Human Albumin 4%) & ALBUMEX® 20 (Human Albumin 20%) Indications: ALBUMEX 4 - Hypovolaemia/shock; Cardiopulmonary bypass; Plasma exchange. ALBUMEX 20 - Hypoproteinaemia in the acutely ill patient; Shock; Burns; Adult respiratory distress syndrome (ARDS); Haemodialysis; Plasma exchange. Contraindications: ALBUMEX 4 & ALBUMEX 20 - Cardiac failure, pulmonary oedema, severe anaemia or history of allergy to albumin. ALBUMEX 20 - chronic nephrosis, or hypoproteinaemic states associated with chronic cirrhosis, malabsorption, protein losing enteropathies, pancreatic insufficiency or undernutrition. Precautions: ALBUMEX 4 & ALBUMEX 20 - Circulatory overload may occur, especially in patients with a history of cardiac failure, pulmonary oedema, or who have renal insufficiency, severe or stabilised chronic anaemia or on cardiopulmonary bypass if dosage and rate of infusion are not adjusted to patient's circulatory situation. Cease infusion at first sign of circulatory overload. Blood pressure rises can occur after rapid administration; monitor bleeding points. The use of albumin for fluid resuscitation of patients with traumatic brain injury is not recommended.* Allergic reactions occur rarely; treat by stopping the infusion and administering adrenaline, hydrocortisone and antihistamines as appropriate. Contains trace amounts of aluminium (≤200 mcg/L); consider possible risk of aluminium accumulation when large albumin volumes are comtemplated in chronic renal insufficiency. Administration can aggrevate myocardial depression in shock. Use in pregnancy, lactation, paediatrics or the elderly has not been established in clinical trials. ALBUMEX 4 and ALBUMEX 20 does not contain an antimicrobial preservative, therefore must be used immediately after the container has been entered. ALBUMEX 4 and ALBUMEX 20 is made from human plasma. Products made from human plasma may contain infectious agents, such as viruses and theoretically Creutzfeldt - Jakob Disease agents that can cause disease. The risk that such products will transmit an infectious agent has been reduced by screening plasma donors and by dedicated virus removal and inactivation procedures included in the manufacturing process. Despite these measures, such products may still potentially transmit disease. Vaccination for patients in receipt of medicinal products from human plasma should be considered where appropriate. ALBUMEX 4 - Hypotension has been associated with albumin solutions. ALBUMEX 20 - As ALBUMEX 20 is hyperoncotic, it must be given with, or followed by a crystalloid solution in the presence of dehydration. Sodium content needs to be considered in certain patients (ALBUMEX 20 contains sodium 48-100 mmol/L). Paradoxical refractory oliguria has been reported in burns patients. Interactions: Angiotensin converting enzyme inhibitors. ALBUMEX 4 and ALBUMEX 20 should also not be mixed with protein hydrolysates or solutions containing amino acids, alcohol or drugs that bind to albumin e.g. calcium channel blockers, antibiotics and benzodiazepines. The addition of other drugs has not been evaluated. Adverse Effects: ALBUMEX 4 & ALBUMEX 20 - Uncommon and usually mild and transient with albumin solutions in general, including hypotension, chills, fever and allergic reactions including anaphylaxis, urticaria, skin rashes, pruritis, nausea/vomiting, flushing, dizziness, tachycardia, pyrexia, dyspnoea, and increased salivation. Very rarely, severe allergic reactions may occur. ALBUMEX 20 – hypertension, decreased oxygen saturation and muscle spasms. Overall a low number of post-marketing reports have been received for current generation ALBUMEX 4 and ALBUMEX 20 products. For further details see full Product Information. Dosage & Administration: ALBUMEX 4 - Hypovolaemia/shock: usually at least one litre of ALBUMEX 4 for adults, however the total volume required cannot be accurately predicted as depends on such factors as the initial extracellular fluid volume and the rate of fluid loss. Plasma exchange: infusion rate should be adjusted to match the rate of removal. ALBUMEX 20 - Varies with condition treated and patient's weight. Hypoproteinaemia in the acutely ill patient: 50–75 g/day at a rate not exceeding 2 mL/min; Shock: 20g at a rate of 2–4 mL/min. Infusion rate may be increased in emergencies and repeated every 15-30 min if necessary. Total dose should not exceed the normal albumin levels ie. about 2g/kg in the absence of active bleeding. Administer concentrated albumin solutions (>5%) with a crystalloid solution to prevent tissue dehydration; Burns: 20–80 g/day at a rate of 1mL/min; ARDS: commence with 50 g over first 24 hrs together with diuretic therapy. Thereafter, dose is adjusted to maintain vital signs; Haemodialysis: patients with fluid overload prior to dialysis may benefit from administration of 20-40 g at end of procedure; ALBUMEX 4 & ALBUMEX 20 - Plasma exchange: replace albumin removed on a gram-for-gram basis. If dilution of ALBUMEX 20 is required, use a crystalloid solution (i.e. 0.9% saline), not water. Administered intravenously. Based on ALBUMEX 4 and ALBUMEX 20 Product Information TGA approved 12 September 2011. (Version 09/11)

* Please note change(s) in Product Information

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