



Red Blood Cell Products, Leukocyte Reduced (LR)

This component information addresses:

- **AS-3 Red Blood Cells LR**

Composition and properties

AS-3 Red Blood Cells LR is a red cell concentrate prepared from approximately 450mL whole blood collected in 63mL of CP2D anticoagulant. The unit is plasma reduced by centrifugation and leukoreduced by filtration. Red blood cells are re-suspended in approximately 100mL of AS-3 additive solution.

Note:

CP2D (citrate phosphate dextrose) anticoagulant contains sodium citrate 26.3g/L, citric acid 3.27g/L, monobasic sodium phosphate 2.22g/L and dextrose 51.1g/L.

AS-3 additive solution contains dextrose 11.0g/L, adenine 0.30g/L, monobasic sodium phosphate 2.76g/L, sodium chloride 4.10g/L, sodium citrate 5.88g/L, citric acid 0.42g/L.

TABLE 1: Typical unit content is based on the number of units (n) tested from October 2007 to March 2008, inclusive.

AS-3 Red Blood Cells LR	Volume (mL) Mean ± 2sd n = 3335	Hemoglobin (g/unit) Mean ± 2sd n = 1508	Hematocrit (L/L) Mean ± 2sd n = 1508	Residual Leukocytes (x10 ⁶ /unit) Mean ± 2sd n = 3420
	313 ± 56 n = 3335	58 ± 12 n = 1508	0.56 ± 0.07 n = 1508	0.42 ± 1.41 n = 3420

Quality criteria that must be met in all units tested: Volume: ± 10% labelled volume; Hb: ≥45g/unit; Hct: 0.50-0.70 L/L; Residual Leukocytes: <5x10⁶/unit in all units tested.

Note: 58g Hb approximates to 197mg iron/unit.^{1,2}

The donor sample is tested for ABO group, Rh type and unexpected antibodies against red cell antigens. ABO, Rh and, if present, antibody identity are indicated on the component label.

Prior to making blood components available for transfusion, a sample of each donor's blood must test negative for:

- antibodies to human immunodeficiency virus (HIV-1 and HIV-2), hepatitis C virus (HCV), human T-cell lymphotropic virus, type I and II (HTLV-I/II), hepatitis B core antigen (HBcore)
- hepatitis B surface antigen (HBsAg)
- presence of viral RNA [HIV-1, HCV and West Nile Virus (WNV)]
- syphilis

In some cases, a donor sample is also tested for cytomegalovirus (CMV) antibody and/or the presence of IgA; if negative this is indicated on the label. Known red cell phenotypes will be indicated on the label.

In some emergency situations, with the approval of both the Canadian Blood Services and attending physician, partially tested or untested blood may be released for transfusion.

Packaging

AS-3 Red Blood Cells LR is stored in di-ethyl hexyl phthalate (DEHP) plasticized bags³.

Storage and handling

AS-3 Red Blood Cells LR must be stored at 1 - 6°C. The shelf life is 42 days, unless otherwise specified.

AS-3 Red Blood Cells LR is stored in a closed system. Once the bag is breached, transfuse within 24 hours if maintained at 1 - 6°C or within 4 hours if stored above 6°C.

Visual inspection should occur. A red blood cell unit should be mixed thoroughly prior to transfusion.

Action

Transfused red blood cells increase the oxygen-carrying capacity of the blood by increasing the circulating red blood cell mass.

Indications

AS-3 Red Blood Cells LR is indicated for supplementing oxygen-carrying capacity and for red blood cell replacement in exchange transfusions.

Alternatives to transfusion should be considered prior to the transfusion of red blood cells.

Contraindications

AS-3 Red Blood Cells LR is not suitable for clinical situations where limited oxygen-carrying capacity is not due to red blood cell deficiency or dysfunction.

Warnings and Precautions

Red blood cells must be ABO-compatible. Pre-transfusion testing is required unless withholding blood might result in loss of life.⁴ Except in special circumstances, Rh negative recipients should receive Rh negative red cells.

The intended recipient must be properly identified before the transfusion is started.

Alloimmunisation of the recipient may be a consequence of transfusion.

AS-3 Red Blood Cells LR less than 7 – 14 days old should be considered when large volumes are transfused rapidly to neonates and infants.⁵ Theoretical calculations suggest that, in some settings of massive transfusion in the neonate, infusion of the quantities of constituents found in additive solutions should be avoided. In these settings it may be prudent to remove the supernatant additive solution and resuspend the red cells in the fluid that is most appropriate for the procedure. However there are anecdotal reports of the use of additive solutions in large-volume transfusions in neonates without adverse effect.

Red blood cells should not be the only fluid used in volume resuscitation or massive transfusion.

Patients being transfused with large volumes of red blood cells should be monitored for circulatory overload and other complications of massive transfusion.

Careful donor selection and available laboratory tests do not eliminate the hazard of transmitting infectious disease agents for which testing is performed (see Table 2)⁶ or for pathogens that are either not recognized or for which there is no donor screening test.

TABLE 2: Estimated residual risk of transfusion-transmitted viral infections in Canada with incidence rates from observed donor seroconversions, 2001 to 2005.⁷

Virus	Residual risk	
	Per million donations (95% CI)	Per number of donations
HIV	0.13 (0.05-0.28)	1 in 7.8 million
HCV	0.43 (0.27-0.66)	1 in 2.3 million
HBV	6.55 (3.90-10.29)	1 in 153,000
HTLV*	0.23 (0.04-0.83)	1 in 4.3 million‡

*95 percent CI is not available for HTLV window period, the listed numbers in brackets are the range.

‡This estimate represents potentially infectious units released into inventory. The risk to recipients would be much lower due to universal leukoreduction.

For some patients at particularly high risk of severe CMV disease (e.g. fetus requiring an intrauterine transfusion [IUT], or CMV-seronegative recipients of allogeneic, hematopoietic stem cell transplants from CMV-seronegative donors), clinicians may choose, in addition to the use of LR components, to transfuse components from CMV-seronegative donors.

Some collection needles are in contact with latex. Canadian Blood Services cannot guarantee that this component is latex free.

Adverse events

Potential adverse events related to a blood transfusion range in severity from minor with no sequelae to life-threatening. All adverse events

occurring during a transfusion should be evaluated to determine whether or not the transfusion can be safely continued/restarted. All adverse events suspected to be related to a transfusion (whether during or after a transfusion) should be reported to your local transfusion service and when required (i.e. when the adverse event could be attributed to the quality of a blood component), to Canadian Blood Services and the hospital/regional hemovigilance network. Canadian Standards Association requires reporting of adverse events associated with blood component quality (e.g.: bacterial contamination) to Canadian Blood Services.^{4,8} For further information, refer to the Canadian Standards Association, *Blood and Blood Components*, Section 17.2.2. and Transfusion Transmitted Injuries Surveillance System.^{4,9}

TABLE 3: The following adverse events have been described with transfusions of red blood cell components:^{8,10,11,12,13,14}

Event	Approximate Frequency	Symptoms and Signs	Notes
Mild allergy	1 in 100	Urticaria, pruritis and/or erythema.	Transfusion can be restarted after assessment and necessary intervention.
Febrile non-hemolytic transfusion reactions (FNHTR)	1 in 500	Fever, chills and/or rigor.	Diagnosis of exclusion. A patient with fever should be evaluated for other more serious transfusion reactions.
Transfusion associated circulatory overload (TACO)	1 in 700	Dyspnea, orthopnea, cyanosis, tachycardia, raised venous pressure and/or hypertension.	Due to excessive volume or excessively rapid transfusion rates. May be difficult to distinguish from TRALI.
Transfusion related acute lung injury (TRALI)	1 in 5,000	New onset of hypoxemia, new bilateral lung infiltrates on chest X-ray and no evidence of circulatory overload.	Occurs during or within 6 hours of transfusion. May be difficult to distinguish from TACO.
Delayed hemolytic transfusion reactions (HTR)	1 in 7,000	Hemoglobin levels fall 4 – 14 days post transfusion.	Direct antiglobulin test may be positive. Usually due to an anamnestic response.
Immediate hemolytic transfusion reactions (HTR)	1 in 40,000	Fever, chills, hemoglobinuria, dyspnea, shock, disseminated intravascular coagulation, chest pain, and/or back pain.	Often due to undetected serological incompatibility or sample misidentification.
Bacterial contamination	1 in 50,000 (see explanation in Notes)	Fever, chills, rigors, nausea, vomiting, diarrhea, abdominal and muscle pain, hypotension, hemoglobinemia, and/or disseminated intravascular coagulation.	Approximate risks per red cell unit are: <ul style="list-style-type: none"> • bacterial contamination 1 in 50,000. • bacterial sepsis 1 in 100,000. • death from bacterial sepsis 1 in 500,000. For evaluation and treatment of a reaction due to suspected bacterial contamination, refer to reference #8.
Isolated hypotensive reaction	Unknown	Hypotension, occasionally accompanied by urticaria, dyspnea or nausea.	Diagnosis of exclusion. May occur more frequently in patients on angiotensin-converting enzyme (ACE) inhibitor.
Non-immunologic hemolysis	Uncommon	Fever, chills, hemoglobinuria, chest pain, back pain, dyspnea, shock, disseminated intravascular coagulation and/or renal failure.	Due to simultaneous administration of a hypotonic fluid with transfusion, bacterial contamination or hemolysis from improper handling of the blood, e.g. freezing or overheating.
Anaphylaxis	Rare	Hypotension, upper and/or lower respiratory obstruction, anxiety, nausea and vomiting.	Resuscitation according to institutional guidelines. IgA deficient patients who have formed anti-IgA antibodies may experience anaphylactic reactions. However, in most cases of anaphylactic reactions, no specific antibodies are found in the patient.
Post Transfusion Purpura (PTP)	Rare	Abrupt onset of severe thrombocytopenia 1 – 24 days post transfusion.	Most cases of PTP occur in recipients who are HPA-1b homozygous receiving HPA-1a positive blood components.
Transfusion-related alloimmune thrombocytopenia	Rare	Abrupt onset of potentially severe thrombocytopenia within hours of transfusion.	Passive transfer of platelet antibodies leading to thrombocytopenia.
Graft-versus-host disease (GVHD)	Rare	Pancytopenia, rash, liver dysfunction, diarrhea.	Irradiated cellular blood components eliminate this risk.
Infectious disease	See Table 2, Residual risk of tested viruses	Variable according to infectious disease.	Blood components have been described to transmit viruses other than HIV, HBV, HCV, HTLV/II and WNV as well as parasites and prions.
Iron overload	Dependent on clinical situation	Early stages may be asymptomatic. Clinical signs relate to hepatic, pancreatic and/or cardiac organ damage.	Due to repeated red blood cell transfusions.
Hyperkalemia	Dependent on clinical situation	Cardiac arrhythmia, changes in ECG and/or cardiac arrest.	Seen in massive, rapid transfusion; neonates and infants receiving red cells irradiated prior to storage are at particular risk.
Other complications of massive transfusion	Dependent on clinical situation	Complications may include hypothermia, citrate toxicity, acidosis, dilutional coagulopathy.	Appropriate monitoring may abrogate some complications.

Reporting of suspected cases of transfusion-related infections such as HIV, HCV, HTLV, HBV, WNV and other transfusion-related infections is described in the Clinical Guide to Transfusion, section 1: Vein to Vein: A Summary of Blood Collection and Transfusion in Canada.

Dose and administration

Clinical signs and symptoms of hypoxia, ongoing blood loss and risk of anemia to the patient need to be considered when determining dose. Each unit should raise the hemoglobin concentration in an average size, non-bleeding adult by approximately 10g/L. Common pediatric dosing is 10-15mL per kg body weight. Alternatively, the following formula could be used:¹⁵

$$\text{Volume to transfuse} = 0.5 \times (\text{desired Hb} - \text{current Hb}) \times \text{patient weight}$$

Volume in mL; Hb in g/L; weight in kg

A standard blood administration set containing a 170 – 260 micron filter or a filter of equivalent efficacy, approved by Health Canada, must be used for infusion. A blood warmer licensed by Health Canada for that purpose may be used at the discretion of the attending physician.

No medications or solutions, with the exception of 0.9% sodium chloride, may be added to or infused through the same tubing with **AS-3 Red Blood Cells LR**. In particular, the addition of commonly used solutions such as D5W (5% dextrose in water) or additives such as calcium (e.g. in Lactated Ringers), should never be added to, or administered concurrently through the same vascular access as blood or blood components. Co-administration of ABO-compatible plasma or 5% albumin can be performed at the discretion of the treating physician.

Transfusion rate is dependent on clinical factors. For more information, refer to the Clinical Guide to Transfusion. All transfusions should be complete within 4 hours of removal from storage. Patients should be under clinical observation, in accordance with institutional guidelines, during transfusion with close observation during the first 15 minutes.

Modifications and additional information

Modification	Description	Indication	Storage	Benefits	Adverse events
Washed	Most of the plasma is removed; unit contains at least 75% of red blood cells from original unit after washing.	<ul style="list-style-type: none"> IgA-deficient recipient with anti-IgA severe or repeated allergic reactions to blood components, unresponsive to pre-medication. 	1 - 6°C: transfuse within 24 hours. 20 - 24°C: transfuse within 4 hours.	Less frequent febrile non-hemolytic and allergic reactions.	As per Table 3. Slightly increased risk for bacterial contamination.
Deglycerolized (frozen/thawed)	Glycerol added and unit frozen within 14 days of collection. Once thawed, washing removes glycerol and supernatant fluid; contains >80% of red blood cells from original cryopreserved unit, hematocrit <0.80L/L. The suspension medium, unless otherwise specified on the label, is 0.9% Sodium Chloride Injection (USP), with or without small amounts of dextrose. A pink-tinged supernatant after washing is acceptable for transfusion, otherwise return unit to blood bank.	Red Blood Cells for patients requiring specific or rare phenotypes not available in liquid inventory.	Store frozen up to 10 years. 1 - 6°C: transfuse within 24 hours. 20 - 24°C: transfuse within 4 hours.	Permits prolonged storage of rare blood types.	As per Table 3. Intravascular hemolysis due to residual glycerol; slightly increased risk for bacterial contamination.
Irradiation ¹⁶	Cells are exposed to gamma irradiation.	Recipients who are immunocompromised or who receive units from closely matched HLA or related/directed donor.	1 - 6°C: 28 days post-irradiation or original expiry date, whichever comes first.	Eliminates risk of GVHD.	As per Table 3. Increased risk of hyperkalemia with prolonged storage following irradiation.
Divided	An integral satellite pack is attached to facilitate transfusion of aliquots.	Neonates.	1 - 6°C: 42 days, unless otherwise specified.	Reduced donor exposure.	As per Table 3.

Autologous Donations

Autologous donor samples are typically tested as described above. Syphilis and anti-HBcore are not mandatory tests for autologous donations.⁴ Autologous units found to be repeat reactive, but negative/indeterminate on confirmatory/supplemental testing for any of the transmissible disease markers will be labeled as “Biohazard” and providing all other requirements have been met, may be released with the approval of both the Canadian Blood Services and attending physician. In addition, syphilis confirmatory positive units may also be released with “Biohazard” labelling.

Directed Donations

Directed donations are donations made by a donor chosen for or by the recipient. This type of donation is offered in specific and limited cases and may be given only by parents or legal guardians to their minor children. A directed red cell unit must meet all the standards required for **AS-3 Red Blood Cells LR**.

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The Circular as a whole or in part cannot be considered or interpreted as an expressed or implied warranty of the safety or fitness of the described blood or blood components when used for their intended purpose. Attention to the specific indications for blood components is needed to prevent inappropriate transfusion.



Canadian Blood Services
it's in you to give

Canadian Blood Services
1800 Alta Vista Drive
Ottawa, Ontario, Canada
K1G 4J5

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This *Circular* is an extension of the component label and conforms to the applicable Regulations issued by the Health Products and Food Branch, Health Canada.¹⁷