Red Blood Cells, Leukocytes Reduced (LR)

This component information addresses:

- Red Blood Cells LR SAGM added

Composition and properties

Red Blood Cells LR SAGM added is a red cell concentrate prepared from approximately 480 mL of whole blood collected in 70 mL of CPD anticoagulant. The unit is plasma reduced by centrifugation, platelet reduced by either centrifugation or filtration and leukoreduced by filtration. Each unit contains a maximum of 29 mL of plasma and approximately 110 mL of SAGM additive.

Notes:
CPD (citrate, phosphate, dextrose) anticoagulant contains citric acid 3.27 g/L, sodium citrate 26.3 g/L, sodium acid phosphate 2.51 g/L, dextrose 25.5 g/L.
SAGM (pyruvate, adenine, glucose, mannitol) additive solution contains sodium chloride 8.77 g/L, dextrose 9.00 g/L, adenine 0.169 g/L, mannitol 5.25 g.L.

<table>
<thead>
<tr>
<th>Red Blood Cells LR SAGM added</th>
<th>Volume (mL)</th>
<th>Mean ± 2 SD</th>
<th>Hemoglobin (g)</th>
<th>Mean ± 2 SD</th>
<th>Hematocrit (L/L)</th>
<th>Mean ± 2 SD</th>
<th>Residual Leukocytes (x10⁶)</th>
<th>Mean ± 2 SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>304 ± 61</td>
<td>57 ± 16</td>
<td>0.65 ± 0.08</td>
<td>0.32 ± 8.20</td>
<td>13918</td>
<td>13918</td>
<td>n = 13918</td>
<td>n = 13918</td>
</tr>
</tbody>
</table>

Quality criteria that must be met:
Volume: ±10% labelled volume; Hb: ≥40 g/unit in 90% of units tested; Residual Leukocytes: <5x10⁶/unit in all units tested.

The donor sample is only tested 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) and hepatitis B surface antigen (HBsAg).

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

A donor sample is only tested for antibodies to Trypanosoma cruzi (T. cruzi or Chagas Disease) when increased risk is present.

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

Packaging

Red Blood Cells LR SAGM added, are stored in di-ethyl hexyl phthalate (DEHP) plasticized bags.1,2,4 Segments containing red blood cells and plasma but no SAGM are yellow in colour; segments containing red blood cells, SAGM and residual plasma can vary in colour from pale yellow to a slight pink tinge (due to red blood cells settling out of SAGM).

Storage and handling

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

Once the bag is breached, the unit should be transfused within 24 hours if maintained at 1 - 6°C or within 4 hours if stored above 6°C.

Visual inspection should be performed; refer to the Visual Assessment Guide for further information.5 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

Red Blood Cells LR SAGM added 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

Red Blood Cells LR SAGM added 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.7 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.

Alloimmunization of the recipient may be a consequence of transfusion.

Red Blood Cells LR SAGM added less than 7 – 14 days old should be considered when large volumes are transfused rapidly to neonates and infants.8 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)9 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, 2006 to 2009. ¹ ²

<table>
<thead>
<tr>
<th>Virus</th>
<th>Residual risk</th>
<th>Per million donations (95% CI)</th>
<th>Per number of donations</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>0.12 (0.07-0.29)</td>
<td>1 in 8 million</td>
<td></td>
</tr>
<tr>
<td>HCV</td>
<td>0.15 (0.09-0.25)</td>
<td>1 in 6.7 million</td>
<td></td>
</tr>
<tr>
<td>HBV*</td>
<td>0.60 (0.30-1.19)</td>
<td>1 in 1.7 million</td>
<td></td>
</tr>
<tr>
<td>HTLV*I</td>
<td>0.41 (0.08-1.19)</td>
<td>1 in 2.5 million</td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted for transient nature of HBsAg by the formula of Korhonen with further adjustment to account for the improved sensitivity of newer HBsAg assays.
‡Canadian Blood Services, National Epidemiology and Surveillance. 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. ³ "For further information, refer to the Canadian Standards Association, Blood and Blood Components and Transfusion Transmitted Injuries Surveillance System."³

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**TABLE 3: The following adverse events have been described with transfusion of red blood cell components.**¹¹,¹³,¹⁴,¹⁵,¹⁶,¹⁷

<table>
<thead>
<tr>
<th>Event</th>
<th>Approximate Frequency</th>
<th>Symptoms and Signs</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild allergy</td>
<td>1 in 100</td>
<td>Urticaria, pruritis and/or erythema.</td>
<td>Transfusion can be restarted after assessment and necessary intervention.</td>
</tr>
<tr>
<td>Febrile non-hemolytic transfusion reactions (FNHTR)</td>
<td>1 in 500</td>
<td>Fever, chills and/or rigor.</td>
<td>Diagnosis of exclusion. A patient with fever should be evaluated for other more serious transfusion reactions.</td>
</tr>
<tr>
<td>Transfusion associated circulatory overload (TACO)</td>
<td>1 in 750</td>
<td>Dyspnea, orthopnea, cyanosis, tachycardia, raised venous pressure and/or hypertension.</td>
<td>Due to excessive volume or excessively rapid transfusion rates. May be difficult to distinguish from TRALI.</td>
</tr>
<tr>
<td>Transfusion related acute lung injury (TRALI)</td>
<td>1 in 5,000</td>
<td>New onset of hypoxemia, new bilateral lung infiltrates on chest X-ray and no evidence of circulatory overload.</td>
<td>Occurs during or within 6 hours of transfusion. May be difficult to distinguish from TACO.</td>
</tr>
<tr>
<td>Delayed hemolytic transfusion reactions (HTR)</td>
<td>1 in 7,000</td>
<td>Hemoglobin levels fall 4 – 14 days post transfusion.</td>
<td>Direct antiglobulin test may be positive. Usually due to an amnestic response.</td>
</tr>
<tr>
<td>Immediate hemolytic transfusion reactions (HTR)</td>
<td>1 in 40,000</td>
<td>Fever, chills, hemoglobinuria, dyspnea, shock, disseminated intravascular coagulation, chest pain and/or back pain.</td>
<td>Often due to undetected serological incompatibility or sample misidentification.</td>
</tr>
<tr>
<td>Bacterial contamination</td>
<td>1 in 50,000 (see explanation in Notes)</td>
<td>Fever, chills, rigor, nausea, vomiting, diarrhea, abdominal and muscle pain, hypotension, hemoglobinuria, and/or disseminated intravascular coagulation.</td>
<td>Approximate risks per red cell unit are: • bacterial contamination 1 in 50,000. • bacterial sepis 1 in 250,000. • death from bacterial sepsis 1 in 500,000. For evaluation and treatment of a reaction due to suspected bacterial contamination, refer to reference #11.</td>
</tr>
<tr>
<td>Isolated hypotensive reaction</td>
<td>Unknown</td>
<td>Hypotension, occasionally accompanied by urticaria, dyspnea or nausea.</td>
<td>Diagnosis of exclusion. May occur more frequently in patients on angiotensin-converting enzyme (ACE) inhibitor.</td>
</tr>
<tr>
<td>Non-immunologic hemolysis</td>
<td>Uncommon</td>
<td>Fever, chills, hemoglobinuria, chest pain, back pain, dyspnea, shock, disseminated intravascular coagulation and/or renal failure.</td>
<td>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.</td>
</tr>
<tr>
<td>Anaphylaxis</td>
<td>Rare</td>
<td>Hypotension, upper and/or lower respiratory obstruction, anxiety, nausea, vomiting.</td>
<td>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.</td>
</tr>
<tr>
<td>Post transfusion purpura (PTP)</td>
<td>Rare</td>
<td>Abrupt onset of severe thrombocytopenia 1 – 24 days post transfusion.</td>
<td>Most cases of PTP occur in recipients who are HPA-1b homozygous receiving HPA-1a positive blood components.</td>
</tr>
<tr>
<td>Transfusion-related alloximmune thrombocytopenia</td>
<td>Rare</td>
<td>Abrupt onset of potentially severe thrombocytopenia within hours of transfusion.</td>
<td>Passive transfer of platelet antibodies leading to thrombocytopenia.</td>
</tr>
<tr>
<td>Graft-versus-host disease (GVHD)</td>
<td>Rare</td>
<td>Pancytopenia, rash, liver dysfunction, diarrhea.</td>
<td>Irradiated cellular blood components eliminate this risk.</td>
</tr>
<tr>
<td>Infectious disease</td>
<td>See Table 2: Residual risk of tested viruses</td>
<td>Variable according to infectious disease.</td>
<td>Blood components have been described to transmit viruses other than HIV, HBV, HCV, HTLV III and WNV as well as parasites and prions.</td>
</tr>
<tr>
<td>Iron overload</td>
<td>Dependent on clinical situation</td>
<td>Early stages may be asymptomatic. Clinical signs relate to hepatic, pancreatic and/or cardiac organ damage.</td>
<td>Due to repeated red blood cell transfusions.</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>Dependent on clinical situation</td>
<td>Cardiac arrhythmia, changes in ECG, and/or cardiac arrest.</td>
<td>Seen in massive, rapid transfusion; neonates and infants receiving red cells irradiated prior to storage are at particular risk.</td>
</tr>
<tr>
<td>Other complications of massive transfusion</td>
<td>Dependent on clinical situation</td>
<td>Complications may include hypothermia, citrate toxicity, acidosis, dilutional coagulopathy.</td>
<td>Appropriate monitoring may abrogate some complications.</td>
</tr>
</tbody>
</table>
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 10 g/L. Common pediatric dosing is 10-15 mL per kg body weight. Alternatively, the following formula could be used:\(^18\)

\[
\text{Volume to transfuse} = 0.5 \times (\text{desired Hb} – \text{current Hb}) \times \text{patient weight (kg)}
\]

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 recipient’s physician.

No medications or solutions, with the exception of 0.9% sodium chloride injection, may be added to or infused through the same tubing with Red Blood Cells LR SAGM added. 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 recipient’s 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.

**Modification and additional information**

<table>
<thead>
<tr>
<th>TABLE 4: Modified Components</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Modification</strong></td>
</tr>
<tr>
<td>Washed</td>
</tr>
<tr>
<td>Extra Wash (IgA deficient)</td>
</tr>
<tr>
<td>Deglycerolized (frozen/thawed)</td>
</tr>
<tr>
<td>Irradiation(^9)</td>
</tr>
<tr>
<td>Divided</td>
</tr>
</tbody>
</table>

Note: The deglycerolization process of red blood cells collected in anticoagulants other than SAGM will remain the same with the suspension medium, unless otherwise specified on the label, being 0.9% sodium chloride injection, with or without small amounts of dextrose.

**Autologous Donations**

Autologous donor samples are typically tested as described previously. Syphilis and anti-HBc are not mandatory tests for autologous donations.\(^7\) Autologous units found to be repeat reactive, but negative/indeterminate on confirmatory/supplemental testing for any of the transmissible disease markers will be labelled as “Biohazard” and providing all other requirements have been met, may be released with the approval of both Canadian Blood Services and recipient’s 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 blood cell unit must meet all the standards required for Red Blood Cells LR SAGM added.
References


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.

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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.