7.0 APPROPRIATE USE OF MANUFACTURED BLOOD PRODUCTS

### Policy

The Transfusion Medicine Service follows established guidelines for use of all blood products.

### Reason

- Assist in the efficacious use of blood products
- Improve patient safety by providing the appropriate product at the right dosing schedule

### Patient population

As indicated in subsequent sections concerning individual products

### Responsibilities of the Medical Director, Transfusion Medicine

- Be familiar with the appropriate use of these products
- Assist in utilization management of these blood products by:
  - Developing policies, processes and procedures to screen requests for these products to ensure that the most appropriate product is used in the right dose
  - Promote education of clinical and other staff in the appropriate use of these products
  - Assist clinicians when orders deviate from established guidelines and dose recommendations

### Responsibilities of the treating physician

- Obtain any necessary authorization or special product release

### Responsibilities of Transfusion Medicine Service staff

- Follow associated technical procedures as written
- Consult with the Medical Director, Transfusion Medicine (or delegate) as indicated in procedures, as necessary based on technologist’s skills and experience, or on the basis of available clinical or laboratory information
- Report all instances where these products were not given to a patient who met criteria
- Provide any required request forms and/or contact information needed to obtain appropriate authorization

### Associated documents

Ontario guidelines have been developed for the following:
- IVIG
- Albumin

Refer to: [www.transfusionontario.org](http://www.transfusionontario.org)

National guidelines have been developed for the following:
- Prothrombin Complex concentrates (PCC)
- Solvent/detergent-treated plasma
- Recombinant FVIIa
- Fibrinogen Concentrates

Refer to: [www.nacblood.ca](http://www.nacblood.ca)

7.1 APPROPRIATE USE OF PLASMA FRACTIONATED PRODUCTS

 Plasma fractionated products include:

- Albumin
- Intravenous immunoglobulin (IVIG)
- Subcutaneous immunoglobulin
- Specific immune globulins (RhIG, SCIG, HepBIG, VZIG)
- Human derived clotting factor concentrates (FEIBA, PCC, FXI, fibrinogen concentrates)
- Recombinant clotting factors (FVII, VIII, IX, FXIII)

7.2 INDICATIONS FOR THE USE OF ALBUMIN

7.3 INDICATIONS FOR THE USE OF INTRAVENOUS IMMUNOGLOBULIN (IG)


**General Pre-requisites and indications for IVIG or SCIG Use:**
1. A diagnosis must be confirmed for all orders.
2. For immune deficiency conditions, serum IgG levels must be clinically assessed to ensure optimum dosing.
3. For all other conditions, IVIG should only be used when other, less expensive, equally safe and efficacious alternatives have failed.
4. There must be regular clinical outcome assessment.
5. For all proposed treatments or course of treatments with IVIG and SCIG the MOHLTC IG Request Form (see below) shall be completed by the requesting physician.
6. All request forms must be reviewed for appropriate indication and dosage interval.
7. Detailed information on all aspects of IG Utilization Management can be found in the Immune Globulin Toolkit prepared by ORBCoN.

**Special Requests for Use in Conditions not on the list of Approved Medical Conditions for IG Use:**
- Subject to screening at the hospital level:
  - IG user hospitals shall select the appropriate physician/committee to review, and where appropriate, approve requests for indications not listed on the MOHLTC IG Request Form
  - The physician appointed to serve as the approving physician (or delegate) shall sign the request form
  - On the request form under the heading “Other” the non-licensed indication shall be entered
- In the event of urgent treatment in a life-threatening situation, the request for IVIG shall be met immediately following verification of appropriate dose

**Approved Indications for IG Treatment**
The clinical indication, dose and duration of therapy must be in accordance with the Ontario IG Utilization Management Guidelines.

**Indications for which IG is NOT recommended nor indicated, or is ineffective:**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Efficacy/Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid Arthritis</td>
<td>Ineffective</td>
</tr>
<tr>
<td>Inclusion Body Myositis</td>
<td>Ineffective</td>
</tr>
<tr>
<td>Chronic Fatigue Syndrome</td>
<td>Ineffective</td>
</tr>
<tr>
<td>Recurrent Spontaneous Abortion</td>
<td>Ineffective</td>
</tr>
<tr>
<td>In Vitro Fertilization/Implantation Procedures</td>
<td>Ineffective</td>
</tr>
<tr>
<td>Sepsis In Critical Care Patients</td>
<td>No large randomized controlled trials to confirm benefit</td>
</tr>
<tr>
<td>Autologous Bone Marrow/Stem Cell Transplant</td>
<td>No benefit</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>Ineffective</td>
</tr>
<tr>
<td>Amyotrophic Lateral Sclerosis</td>
<td>Ineffective</td>
</tr>
</tbody>
</table>
IVIG dose calculation:
- An IVIG Dose Calculator based on adjusted body weight is available to determine the appropriate dose for each individual patient.
- Available at http://ivig.transfusionontario.org and as an application for installation on hand-held electronic devices.
- Based on patient height and weight.
- For IVIG for immunoglobulin replacement, use dose calculator for 1st dose and determine subsequent doses based on the IgG trough level.
- Preparations of immunoglobulin are available from Canadian Blood Services. Dosage is individualized, consult package insert.

REFERENCES
36. United Kingdom Department of Health, Clinical Guidelines for Immunoglobulin, 2nd ed. 2011
70. ORBCoN, Immune Globulin Toolkit for Ontario, 2018.
71. BC PBCO, Intravenous Immune Globulin.
### Table 7.1: Use of Recombinant* and Plasma Derived Products that Do Not require a Special Access program (SAP) Approval

<table>
<thead>
<tr>
<th>Product</th>
<th>Clinical Indication</th>
<th>Standard Dose (Always refer to the product insert for most current information)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antihemophilic factor/Von Willebrand Factor complex Humate P® Wilate®</td>
<td>VonWillebrand’s disease when unresponsive to DDAVP</td>
<td><strong>Minor Bleed:</strong> either product Humate® P 40–50 IU/kg 1 or 2 doses Wilate® 20–40 IU/kg q 12–24 hours <strong>Major Bleed:</strong> Humate P® 40–80 IU/kg q 12–24 hours Wilate® 40–60 IU/kg q 8–12 hours</td>
</tr>
<tr>
<td>Factor VIII concentrate* Refer to the hemophilia centre to determine the appropriate product as this is usually patient specific</td>
<td>Hemophilia A</td>
<td>• 1 U/kg produces 2% increase in factor VIII level • Half life variable depending on product</td>
</tr>
<tr>
<td>Factor IX concentrate*</td>
<td>Hemophilia B (Christmas disease)</td>
<td>• 1 U/kg produces 1% increase in factor IX level • Half life variable depending on product</td>
</tr>
<tr>
<td>Factor XIII Concentrate*</td>
<td>Congenital factor XIII deficiency</td>
<td>Consult package inserts</td>
</tr>
<tr>
<td>Antithrombin III</td>
<td>Antithrombin deficiency  • Congenital deficiency  • Heparin resistance in association with cardiovascular surgery</td>
<td>Refer to package insert.</td>
</tr>
</tbody>
</table>
### 7.0 Appropriate Use of Manufactured Blood Products

<table>
<thead>
<tr>
<th>Resource</th>
<th>Description</th>
<th>Dose/Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rh Immune Globulin (RhIG)</strong></td>
<td>For prevention of RhD alloimmunization in at-risk RhD negative females</td>
<td></td>
</tr>
<tr>
<td>Pregnancy</td>
<td>At 28 weeks gestation and post-partum with RhD positive infant</td>
<td>Dose at 28 weeks, 1,500 IU or 300ug. Dose post-partum, 1,500 IU or 300ug. (may require additional doses as calculated following quantitation of fetomaternal hemorrhage).</td>
</tr>
<tr>
<td>Obstetrical **</td>
<td>Abortion-- therapeutic, spontaneous or threatened</td>
<td>1,500 IU or 300ug</td>
</tr>
<tr>
<td>Amniocentesis or chorionic villus sampling (CVS) &lt;34 weeks gestation</td>
<td>Amniocentesis, CVS or other manipulation &gt;34 weeks gestation</td>
<td>1,500 IU or 300ug</td>
</tr>
<tr>
<td>Additional sensitizing events (e.g. trauma, fall)</td>
<td>Post-transfusion of Rh D positive red blood cells or platelets</td>
<td>600 IU or 120ug</td>
</tr>
<tr>
<td>Varicella-Zoster Immune Globulin (VZIG)</td>
<td>Passive immunization to chickenpox in high risk exposed patients</td>
<td>&lt;12 weeks: 600 IU or 120ug. ≥12 weeks: 1,500 IU or 300ug.</td>
</tr>
<tr>
<td>Hepatitis B Immune Globulin (HBIG)</td>
<td>Passive immunization of exposed patients</td>
<td>1,500 IU or 300ug for each 15mL red blood cells or 30 mL whole blood</td>
</tr>
<tr>
<td>Tetanus Immune Globulin (TIG)</td>
<td>Passive immunization of exposed patients</td>
<td></td>
</tr>
<tr>
<td>Prothrombin Complex Concentrates (Octaplex® and Beriplex®)</td>
<td>Treatment of major bleeding or in anticipation of urgent surgery in acquired deficiency of the prothrombin complex coagulation factors due to vitamin K antagonists or deficiency (for use in pediatric patients - see section 8.4)</td>
<td>Effective half life is only about 6 hours. INR &lt;3 – 1,000 IU. INR 3-5 – 2,000 IU. INR &gt;5 (adults only) 3,000 IU. Adjust for patients with extremes of body weight (&lt;50kg, &gt;90 kg). For details of INR and weight-based dosing see chart available at <a href="http://www.nacblood.ca">www.nacblood.ca</a>.</td>
</tr>
<tr>
<td>C1 esterase inhibitor</td>
<td>Treatment of hereditary angioedema in C1 esterase deficiency</td>
<td>Refer to product insert</td>
</tr>
<tr>
<td>Fibrinogen concentrate (riaSTAP™)</td>
<td>Acquired hypofibrinogenemia</td>
<td>Refer to product insert and <a href="http://www.nacblood.ca">www.nacblood.ca</a></td>
</tr>
</tbody>
</table>
### Table 7.2: Use of Products that Require approval through Health Canada Special Access Program or SAP

[https://www.canada.ca/en/health-canada/services/drugs-health-products/special-access/drugs/special-access-programme-drugs-1.html](https://www.canada.ca/en/health-canada/services/drugs-health-products/special-access/drugs/special-access-programme-drugs-1.html)

<table>
<thead>
<tr>
<th>Plasma Fractionated Product</th>
<th>Clinical Indication</th>
<th>Dose Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor VII concentrate</td>
<td>Congenital FVII deficiency</td>
<td>Refer to product insert</td>
</tr>
<tr>
<td>Factor XI concentrate</td>
<td>Congenital FX deficiency</td>
<td>Refer to product insert</td>
</tr>
<tr>
<td>Factor XIII concentrate</td>
<td>Congenital FXI deficiency</td>
<td>Refer to product insert</td>
</tr>
<tr>
<td>Protein C concentrate</td>
<td>Congenital or acquired deficiency of Protein C</td>
<td>Refer to product insert</td>
</tr>
</tbody>
</table>

### REFERENCES

94. NAC, 2014.

### 7.4 USE OF RECOMBINANT FACTOR VIIA, ERYTHROPOIETIN

**Policy**

The Transfusion Medicine Service follows established guidelines for use and dosage of recombinant products for the purposes outlined below.

The Medical Director, Transfusion Medicine has established a process to screen requests for recombinant products. This process includes creation and maintenance of a record of the patient response to therapy and outcome.

All first time requests for recombinant factors must be approved by the Medical Director, Transfusion Medicine to address the issue of “off-label” use of recombinant factor VIIa.

**Applies to**

- Recombinant Factor VIIa:
  - Control of bleeding in congenital factor VII deficiency
  - Patients with hemophilia A and B with coagulation factor inhibitors
  - Patients with acquired coagulation factor inhibitors refractory to medical therapy
  - Not recommended for treatment of bleeding in patients without the disorders listed above
7.0 APPROPRIATE USE OF MANUFACTURED BLOOD PRODUCTS

Responsibilities of the Medical Director, Transfusion Medicine

- Be familiar with the availability and use of recombinant products and be aware that:
  » NAC guidelines recommend against off label use
  » Random controlled trials do not support off label use
  » Risk of adverse event is doubled over age 65 and tripled over age 75
- Understand the indications for and use of erythropoietin in the management of peri-operative patients and for patients who refuse blood transfusion
- Ensure effective use of recombinant products by:
  » Screening requests for recombinant products
  » Promoting education of treating physicians and other health care professionals in the appropriate use of recombinant products
- Manage the inventory by:
  » Determining if the patient population served warrants holding a supply of these products as part of regular inventory, or should be requested from Canadian Blood Services on an ad hoc basis
  » Ensuring recirculation for expiring products in a timely fashion

Responsibilities of Transfusion Medicine Staff

- Follow associated technical procedures as written
- Respond promptly to requests where there life-threatening hemorrhage
- Insist that proper documentation is followed
- Order, receive and issue recombinant products
- Contact the Medical Director, Transfusion Medicine on receiving first-time requests for recombinant products
- Be aware that for all off-label requests for refractory bleeding:
  » NAC guidelines recommend against off label use
  » Random controlled trials do not support off label use
  » Risk of adverse event is doubled over age 65 and tripled over age 75

Conditions

- Recommended dosing for recombinant factor VIIa for:
  » Inhibitor patients - 70-90u/kg 2 hourly
  » Congenital factor VII deficiency – 15-30u/kg 4-6 hourly

Erythropoietin

Although erythropoietin is not distributed through the Transfusion Medicine Service, the Medical Director, Transfusion Medicine should be familiar with the drug and its indications for use in the peri-operative period and for patients who refuse blood transfusion.

REFERENCES