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 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

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

Refer to Bloody Easy 4: blood transfusions, blood alternatives and transfusion reactions, 4th ed, 2016.

7.3 INDICATIONS FOR THE USE OF INTRAVENOUS IMMUNOGLOBULIN (IG)

In April 2012 the Ontario Ministry of Health and Long Term Care launched their IVIG strategy. For a toolkit and the associated guidelines, refer to http://transfusionontario.org/en/download/immune-globulin-toolkit-for-ontario/

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.
http://transfusionontario.org/en/documents/?cat=utilization-management-guidelines

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

Diagnosis	Efficacy/Comment
Rheumatoid Arthritis	Ineffective
Inclusion Body Myositis	Ineffective
Chronic Fatigue Syndrome	Ineffective
Recurrent Spontaneous Abortion	Ineffective
In Vitro Fertilization/Implantation Procedures	Ineffective
Sepsis In Critical Care Patients	No large randomized controlled trials to confirm benefit
Autologous Bone Marrow/Stem Cell Transplant	No benefit
Epilepsy	Ineffective
Amyotrophic Lateral Sclerosis	Ineffective

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.

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Table 7.1: Use of Recombinant* and Plasma Derived Products that Do Not require a Special Access program (SAP) Approval

<table>
<tr><th>Product</th><th>Clinical Indication</th><th>Standard Dose
(Always refer to the product insert for most current information)</th></tr>
<tr><td>Antihemophiliac factor/ Von Willebrand Factor complex
Humate P®
Wilate®</td><td>VonWillebrand’s disease when unresponsive to DDAVP</td><td>Minor Bleed: either product
Humate® P 40-50 IU/kg 1 or 2 doses
Wilate® 20-40 IU/kg q 12-24 hours

Major Bleed:
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

<table><tr><th>Category of Bleed</th><th>Activity Goal</th></tr><tr><td>mild</td><td>30%</td></tr><tr><td>major</td><td>50-100%</td></tr></table></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

<table><tr><th>Category of Bleed</th><th>Activity Goal</th></tr><tr><td>mild</td><td>30%</td></tr><tr><td>major</td><td>50-100%</td></tr></table></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>
</table>

Rh Immune Globulin (RhIG) **Note: Following any event at 20 weeks gestation or thereafter, feto-maternal testing should be performed to determine if additional doses of RhIG are required**	For prevention of RhD alloimmunization in at-risk RhD negative females _____ Pregnancy • At 28 weeks gestation and post-partum with RhD positive infant _____ Obstetrical ** Abortion-- therapeutic, spontaneous or threatened _____ Amniocentesis or chorionic villus sampling (CVS) <34 weeks gestation _____ Amniocentesis, CVS or other manipulation >34 weeks gestation _____ Additional sensitizing events (e.g. trauma, fall) _____ Post-transfusion of Rh D positive red blood cells or platelets	_____ 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 feto-maternal hemorrhage) _____ 1,500 IU or 300ug _____ 1,500 IU or 300ug _____ 600 IU or 120ug _____ <12 weeks : 600 IU or 120ug ≥ 12 weeks: 1500 IU or 300ug _____ 1,500 IU or 300ug for each 15mL red blood cells or 30 mL whole blood
Varicella-Zoster Immune Globulin (VZIG)	Passive immunization to chickenpox in high risk exposed patients	125 U/10kg to maximum of 625U, within 96 hours of exposure
Hepatitis B Immune Globulin (HBIG)	Passive immunization of exposed patients	Dose 0.06ml/kg immediately Repeat in 1 month if not vaccinated
Tetanus Immune Globulin (TIG)	Passive immunization of exposed patients	For dose, refer to package insert
Prothrombin Complex Concentrates (Octaplex® and Beriplex®)	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)	Effective half life is only about 6 hours INR <3 – 1,000 IU INR 3-5 – 2,000 IU INR >5 (adults only) 3,000 IU Adjust for patients with extremes of body weight (<50kg, >90 kg) For details of INR and weight-based dosing see chart available at www.nacblood.ca
C1 esterase inhibitor	Treatment of hereditary angioedema in C1 esterase deficiency	Refer to product insert
Fibrinogen concentrate (riaSTAP™)	Acquired hypofibrinogenemia	Refer to product insert and www.nacblood.ca

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

Plasma Fractionated Product	Clinical Indication	Dose Information
Factor VII concentrate	Congenital FVII deficiency	Refer to product insert
Factor XI concentrate	Congenital FX deficiency	Refer to product insert
Factor XIII concentrate	Congenital FXI deficiency	Refer to product insert
Protein C concentrate	Congenital or acquired deficiency of Protein C	Refer to product insert

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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

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.

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