Transfusion Best Practice Recommendations in Adult Patients – Saskatchewan

Blood transfusion is the administration of any blood component or fractionated protein product derived from donated human blood given by any route (i.e. intravenous, intramuscular, subcutaneous, topical) to a recipient. It is the most common medical procedure in the hospital setting. The decision to order a blood transfusion should be made carefully, ensuring that transfusion benefits, risks, and alternatives have been considered. It is prudent for the perceived benefit of the blood transfusion to outweigh the risks for the blood transfusion to be justifiable. Informed consent to receive blood must be obtained from the patient by the most responsible practitioner prior to the administration of a blood transfusion.

Blood components and blood products are precious resources, dependent on a voluntary donor base. Therefore, blood is not an infinite resource. Canadian Blood Services collects and manufactures blood components and procures blood products for our healthcare system. Provincial Ministries of Health fund hospital access to blood, which is distributed to patients by local Transfusion Medicine Laboratories. In Canada, there is no personal cost to patients when blood component and blood product transfusion is are necessary for patient treatment.

This document summarizes best practice recommendations for adult patients receiving transfusion of blood components, which include red blood cells (RBC), platelets and plasma. Alternatives to blood component transfusion are discussed, including indications for specific blood products. Recommendations made are in alignment with evidence-based transfusion medicine practices and reflect published national clinical practice guidelines. Specific blood component and blood product details are now available in Transfusion Medicine Product Monographs.

Choosing Wisely Canada and their clinical specialty partners have created recommendations, several of which are used within this document, for reducing unnecessary blood component transfusions. Ensuring appropriateness of blood transfusion has been demonstrated to improve overall patient outcomes and save health system costs. **Using Blood Wisely** is a new initiative by Choosing Wisely Canada and Canadian Blood Services launched in September 2020. The focus of this national campaign is to decrease inappropriateness of red blood cell transfusion practices in Canada. Additional information can be found at https://usingbloodwisely.ca/

As a directive of the Transfusion Medicine Discipline Committee in January 2024, all large and medium size hospitals in Saskatchewan are now required to participate in the Using Blood Wisely program, which includes auditing red blood cell transfusions to ensure transfusion appropriateness.

The Saskatchewan Transfusion Medicine Physicians thank our clinical colleagues for partnering with us to provide only the best transfusion care to our patients.

To consult with an on-call Transfusion Medicine Physician (available 24/7), please call:

- **Saskatoon and Northern Saskatchewan** – 306-655-1000
- **Regina and Southern Saskatchewan** – 306-766-4444

General Transfusion Considerations

- Obtaining and documenting informed patient consent for blood component or blood product transfusion prior to administration is mandatory.
- Pre-transfusion testing (Group and Screen) should be completed prior to blood component transfusion.
    - The Group (ABO Group/Rh Type test) enables issue of ABO/Rh compatible blood components.
    - A Group & Screen and Crossmatch must be requested if RBC transfusion is required.
    - Uncrossmatched red blood cells (RBC) are only used in emergency situations, with clear documentation of indication necessary to justify use.
- Patient identifiers including a patient name and unique identification number (even if temporarily assigned due to unknown patient identity) are required for issue of any blood components or products from the lab.
- In accordance with laboratory accreditation standards, blood transfusion orders must be properly written by the most responsible practitioner and include the following information:
    - Patient identifiers
    - Date/time of the blood request
    - Indication for transfusion
    - Component or product name
    - Dose (number of units or volume)
    - Infusion duration (rate or total number of hours)
    - Sequence of transfusion if multiple units requested
    - Special attributes, if applicable (washed, irradiated; specific equipment required, etc.)
- Pre-medications:
    - Antihistamines should be considered if there is a history of recurrent, severe allergic reaction with previous transfusion.
        - Second generation antihistamines (e.g. cetirizine or loratadine) are preferred as non-sedating medications over diphenhydramine
    - Antipyretics for *prevention* of fever have not been found to be effective and are not recommended.
    - Diuretic administration *before* blood component transfusion should be considered in patients with one or more risk factors for transfusion-associated circulatory overload (TACO), as long as the patient is not hypovolemic or hemodynamically unstable.
        - TACO risk factors include:
            - Acute or chronic renal insufficiency
            - Positive fluid balance
            - Age 70 and over
            - Congestive heart failure or left ventricular dysfunction
            - History of myocardial infarction
- Infusion of blood components must be completed **within 4 hours** of issue from the Transfusion Medicine Laboratory (TML).
    - Blood components can be returned to general inventory if received by the TML **within 60 minutes** of issue.
- Administer each blood component unit (250-300 mL volume per unit of red blood cells (RBC); 200 mL volume per dose platelets or per unit plasma) at a rate appropriate for the patient volume status:
    - Hypovolemic – over 1-1.5 hours
    - Normovolemic – over 2 hours
    - Hypervolemic – over 3-4 hours
- Whenever possible, **all** transfusions should be completed during the day shift, for optimum patient safety.
- Consider tranexamic acid (15 mg/kg IV, up to 2 g IV total bolus dose) in all cases of severe hemorrhage or patients at risk of bleeding. Administration should occur as close to onset of bleeding as possible.
- **All transfusion adverse reactions MUST be reported to the Transfusion Medicine Laboratory (TML).**

Blood Component Compatibilities

ABO Compatibility

Donor-recipient ABO compatibility is dependent on the ABO group of both the recipient and donor to ensure an appropriate blood component is selected for transfusion.

- RBC – possess surface antigens of the ABO Blood Group System (A, B, both or neither), and other minor blood group systems (ex. Rh, Kell, Duffy, etc);
- Plasma – possesses naturally occurring isohemagglutinin antibodies against antigens of the ABO Blood Group System (anti-A, anti-B, both or neither), and may possess antibodies against antigens from minor blood group systems dependent on sensitizing exposure events of the individual.

Recipient ABO Group	Recipient ABO Surface Antigens	Donor RBC Compatibility	Recipient Isohemagglutinin Antibodies	Donor Plasma or Platelet* Compatibility
A	A	A, O	anti-B	A, AB
B	B	B, O	anti-A	B, AB
AB	A and B	AB, A, B, O	None	AB
O	None	O	anti-A and anti-B	O, A, B, AB

***Note: Although every effort is made to issue ABO compatible platelet and cryoprecipitate units, in situations of inventory limitation, transfusion medicine standards permit transfusion of ABO incompatible platelets. This permission DOES NOT apply to RBC and plasma.**

RBC Crossmatch Compatibility

A crossmatch is required for RBC transfusion only. This test is used to detect incompatibilities between donor red blood cells and the recipient plasma. This can be achieved through 3 types of crossmatch which are perfomed by the TML:

- *Immediate Spin (IS) Crossmatch* – Manual test to confirm ABO compatibility only.
    - Completed to verify ABO compatibility prior to RBC issue; only performed if the antibody screen is negative and computer assisted (electronic) crossmatch is not available.
- *Computer Assisted (Electronic) Crossmatch* – Computer selection of appropriate ABO compatible RBC units.
    - Only utilized if the antibody screen is negative.
- *Indirect-antiglobulin test (IAT) crossmatch* – Mandatory in the setting of a positive antibody screen. The test involves incubation of donor RBC, recipient plasma and anti-IgG to enhance the reaction.
    - Designed to identify antibodies against RBC that may be clinically significant and cause a hemolytic transfusion reaction. Auto-antibodies may interfere with testing.

Crossmatch Compatible RBC are the safest for patients requiring RBC transfusion.

- Risk of delayed hemolytic transfusion reaction (DHTR) is ~1:7000

Crossmatch Incompatible RBC are ABO compatible with the patient but crossmatch incompatible due to patient autoantibodies, and have been authorized for administration by the transfusion medicine physician prior to issue. They are safe to administer; careful monitoring is required during infusion. Please see the Provincial Monograph for Red Blood Cells (RBCs) for further details.

Uncrossmatched RBC are issued in an emergency setting, when time does not allow for the antibody screen and a crossmatch to be performed prior to RBC unit issue. Units may be Group O or ABO identical, depending on testing completed by the Transfusion Medicine Lab at the time that blood is required.

- Risk of DHTR is ~1:1000

Red Blood Cells (RBC)

- One RBC unit usually raises the hemoglobin (Hb) by approximately 10 g/L in an average size adult patient, though the degree of Hb rise is dependent upon patient size and overall blood volume or rate of ongoing blood loss.
- Hemoglobin and hematocrit equilibrate rapidly post-transfusion, allowing for a reliable post-transfusion CBC result if collected anytime from 15 minutes to 24 hours following RBC transfusion.
- The RBC unit age (time from collection to transfusion) is irrelevant and does not impact patient outcomes.
- RBC crossmatching **must** be completed within an accredited laboratory by trained Medical Laboratory Technologists.
    - Consult the Saskatchewan *Current State Blood Drop Map* for details regarding existing laboratory service categories, available at the following link: https://saskblood.ca/blood-drop-map/
    - Turn-around time for crossmatched blood is dependent on several factors, including proximity of the closest facility which can perform crossmatch testing, the day of the week and transportation logistics.
        - There may be a delay of up to 72 hours in obtaining crossmatched RBCs for transfusion in rural communities if the specimen must be sent to another testing site.
    - Contact the on-call Transfusion Medicine Physician to discuss urgent RBC transfusion needs in rural communities where on-site RBC crossmatching is unavailable.
- The underlying cause of anemia should be investigated with the intent of avoiding RBC transfusion, if possible.
    - Treat identified nutritional deficiencies (iron, vitamin B12, folate) with the goal of maintaining a hemoglobin of at least 120 g/L in women and at least 130 g/L in men.
- Patients with hemoglobinopathies (ex. sickle cell disease, thalassemia) should only be transfused under the direction of a Hematologist – transfusion may sometimes be absolutely contraindicated in these patients.
- **The patient clinical context and other causes of anemia signs/symptoms *must* be considered and excluded before administration of RBC transfusion.**
    - Signs/symptoms of anemia may include:
        - Presyncope or syncope;
        - Dyspnea with or without exertion;
        - Tachycardia; chest pain with or without exertion;
        - Severe postural dizziness with hypotension or postural pulse increment of 30 beats/min or more in the setting of significant acute blood loss.

RED BLOOD CELL (RBC) TRANSFUSION – OUTPATIENT	
Clinical Setting	**Recommendation and dose**
Hemoglobin (Hb) 80 g/L or less*	Transfusion of up to 2 units RBC is likely acceptable. If RBC transfusion is given, re-check patient clinical status before giving second unit. Exceptions: • Young patients may tolerate Hb levels under 60 g/L without transfusion. • Patients with chronic iron deficiency anemia without anemia symptoms; IV iron supplementation should be given instead. • Patients with sickle cell disease.
Hb 81-89 g/L*	RBC transfusion likely inappropriate, unless there is symptomatic anemia or clinical evidence of impaired tissue oxygenation.
Hb greater than or equal to 90 g/L*	RBC transfusion likely inappropriate. If transfusion is ordered, clearly document indication in patient's chart and discuss reason with patient.

* Assumes patient is NOT bleeding

- **Outpatient** RBC transfusion for patients with marrow failure related to the underlying diagnosis or chemotherapy may receive up to 2 units RBC for anemia prophylaxis if the pre-transfusion hemoglobin is under 90 g/L.
    - Requests for RBC with a pre-transfusion hemoglobin 90 g/L or higher may be reviewed by the Transfusion Medicine Physician.
- A maximum of 2 units RBC may be transfused in one outpatient appointment. Requests for transfusion of 3 or more RBC units in the outpatient setting may require approval by a Transfusion Medicine Physician.

RED BLOOD CELL (RBC) TRANSFUSION – INPATIENT	
Clinical Setting	**Recommendation and dose**
Hemoglobin (Hb) 55 g/L or less*	Transfusion should be considered. Transfuse 1 unit and re-assess Hb and patient symptoms. Exceptions: • Young patients may tolerate Hb levels under 55g/L without transfusion. • Patients with chronic iron deficiency anemia without anemia symptoms; IV iron supplementation should be given instead.
Hb 70 g/L or less*	Transfusion of 1 unit RBC is likely acceptable. If RBC transfusion is given, re-check patient symptoms and Hb before giving second unit. Exceptions: • Young patients may tolerate Hb levels under 55g/L without transfusion • Patients with chronic iron deficiency anemia without anemia symptoms; IV iron supplementation should be given instead • Patients with sickle cell disease
Hb 75 g/L or less	Patients undergoing cardiac surgery, transfusion of 1 unit RBC is likely acceptable.
Hb 80 g/L or less*	Consider RBC transfusion in patients with pre-existing cardiovascular disease with or without symptoms of anemia, and in perioperative patients with a confirmed hip fracture. Transfuse 1 unit and recheck patient symptoms and Hb before ordering a second unit.
Hb 81-90 g/L*	RBC transfusion likely inappropriate, unless there is symptomatic anemia or clinical evidence of impaired tissue oxygenation. • In patients with Type 1 myocardial infarction (catheter-proven plaque rupture), RBC transfusion may be considered at the discretion of the Cardiologist. There is no benefit of liberal transfusion threshold in other patients with active cardiac ischemia (MINT trial).
Hb greater than 90 g/L*	RBC transfusion likely inappropriate. If transfusion is ordered, clearly document indication in patient's chart and discuss reason with patient.
Bleeding patient	Low cardiovascular risk patient – maintain Hb greater than 70 g/L Pre-existing uncorrected cardiovascular disease – maintain Hb greater than 80g/L

* Assumes patient is NOT bleeding

- Transfusion should not be administered to stable, hospitalized inpatients based on a hemoglobin value alone.
- Inpatient RBC transfusion is indicated for treatment of anemia with clinically significant symptoms.
    - Fatigue alone is not a symptom of anemia which should lead to RBC transfusion.
- For non-bleeding inpatients, the usual adult dose is 1 unit RBC; transfuse 1 unit RBC then re-check Hb and patient symptoms before transfusing a second unit.
- Anticipatory pre-operative RBC transfusion – without medical indication based on the hemoglobin thresholds summarized above, is not recommended.

  - Peri-operative RBC transfusion has been associated with increased patient morbidity and mortality, including in cancer patients undergoing debulking surgery.
  - Patients who are iron deficient should receive peri-operative hemoglobin optimization with supplementation (IV iron is recommended if the patient is in hospital).
  - For Patient Blood Management Resources, please visit: https://saskblood.ca/pbm/

- In the setting of emergency uncrossmatched RBC transfusion, the following RBC will be selected, in accordance with best practice standards:
  - Females of childbearing potential (45 years of age and younger): O negative, Kell negative RBC
  - Males (all) and females older than 45 years of age: O positive RBC

Platelets

- Platelet transfusion is indicated for prophylaxis against bleeding in the setting of hypoproliferative thrombocytopenia or for treatment of acute bleeding in patients with thrombocytopenia or platelet dysfunction. Specific details are included in the table below.
- Platelets are routinely stocked in Saskatoon and Regina only, but can be shipped to any transfusing facility from Canadian Blood Services, upon request.
    - Requests for platelet transfusion in rural facilities for indications other than prophylaxis of bleeding in patients with hypoproliferative thrombocytopenia with a count less than 10 x 10^9/L may be subject to approval by the on-call Transfusion Medicine Physician.
    - Urgent requests for platelets should be discussed with the Transfusion Medicine Physician on-call as transfer of inventory from a tertiary care center may be considered.
- Request for 1 adult dose platelets will lead to issue of any of the following, depending on available inventory:
    - Standard manufacture (non-pathogen inactivated) buffy coat pool (comprised of a pool of 4 donor units) or an apheresis single-donor unit.
    - Psoralen treated/Pathogen Reduced Platelet (PRP), which is pooled (comprised of a pool of 7 donor units suspended in platelet additive solution) or an apheresis single-donor unit.
- Standard manufacture platelets and PRP are considered equivalent in terms of clinical effectiveness.
    - It is acceptable practice to transfuse ABO **in**compatible platelets if compatible platelets are unavailable from the transfusion medicine laboratory due to inventory restrictions. Hemolysis risk is minimal, especially with transfusion of PIT platelets which are resuspended in platelet additive solution rather than donor plasma.
        - Rh negative females 45 years old and younger who receive a platelet transfusion from an Rh positive donor should receive a dose of 120 mcg Rh immune globulin (WinRho) to prevent against RhD alloimmunization.
            - Rh immune globulin prophylaxis is not necessary for Rh negative males (all) or females older than 45 years of age.
- 1 dose of platelets should raise the platelet count by at least 15 x 10^9/L
    - Standard manufacture platelet transfusion often raises the count by approximately 25-40 x 10^9/L; PIT platelets are known to have a lower average post-transfusion platelet increment
    - A post-transfusion CBC should be drawn within 10-60 minutes following the completion of a platelet transfusion to evaluate for an appropriate platelet increment prior to a major procedure, or if there is a clinical concern of platelet refractoriness.
    - If an appropriate increment is not observed, consult the Transfusion Medicine Physician on-call to discuss further testing considerations.
- In patients who are bleeding (regardless of the platelet count), the following aspects should be considered to optimize platelet function:
    - Discontinue antiplatelet agents. Activated charcoal may be administered if ingested less than 4 hours in the setting of active bleeding.
    - Maintain a hematocrit greater than 30% (approximate Hb 90 g/L) and ensure the patient is iron replete.
        - Iron deficiency exacerbates platelet dysfunction.
    - Consider tranexamic acid (15 mg/kg IV, up to 2 g total bolus dose) in all cases of severe hemorrhage or patients at risk of bleeding. Administration should occur as close to onset of bleeding as possible.
    - Consider DDAVP 0.3 mcg/kg up to 20 mcg total dose in patients who are bleeding with:
        - Mild Type 1 Von Willebrand disease, mild Hemophilia A (congenital Factor 8 deficiency) or congenital platelet dysfunction – consult the patient Factor First Card and treat as outlined, then contact the Saskatchewan Bleeding Disorders Program or on-call Hematologist;
        - Uremia due to end stage renal disease.

PLATELET TRANSFUSION – INPATIENT OR OUTPATIENT		
Clinical Setting		**Recommendation and adult dose**
Diagnosis/Indication	**Platelet Count x 10^9/L**	
Asymptomatic patients with chronic bone marrow failure (including those taking low dose oral chemotherapy or azacitidine) or immune thrombocytopenia	Any	No platelet transfusion
Non-immune, hypoproliferative thrombocytopenia due to bone marrow failure on intensive treatment (prophylactic transfusion)	Less than 10	1 dose
Procedures with a low risk† of bleeding, including: • PICC line placement • Tunneled and untunneled central venous line (CVL) placement or removal • Paracentesis, thoracentesis • Endoscopy without biopsy • Bone marrow aspirate and biopsy	Less than 20 Tunneled CVL placement: Less than 20-30	1 dose
Prophylactic anticoagulation that cannot be stopped	Less than 30	1 dose
Therapeutic anticoagulation that cannot be stopped	Less than 30-50	1 dose, and consult thrombosis specialist
Severe, life threatening bleeding	Less than 50	1 dose at a time, clinical judgement and platelet count should guide repeat dosing
Major procedure with a high risk† of bleeding, including: • Lumbar puncture or spinal procedure with hematoma risk • Arterial intervention • Biliary tract intervention or TIPS procedure • Deep abscess drainage • Urinary tract intervention • Solid organ biopsy	Less than 50 Patients with chronic liver disease: Less than 30	1 dose, immediately before procedure, and check platelet response before starting procedure
Epidural anesthesia placement or removal	Less than 70	1 dose, immediately before procedure, and check platelet response before starting procedure
Neurologic bleeding or surgery: • Head trauma or CNS hemorrhage • Neuraxial surgery	Less than 100	1 dose, and check platelet count

Platelet dysfunction **and** significant bleeding • Congenital platelet function defects • Post cardiopulmonary bypass • Life-threatening bleeding with antiplatelet therapy (clopidogrel, ASA 325 mg) ○ *<u>Exceptions</u>: intracranial hemorrhage an no plan for surgery; bleeding due to ticagrelor or anti-GPIIbIIIa antibody*	any	1 dose
Immune thrombocytopenia (ITP) or Thrombotic Thrombocytopenic Purpura (TTP) **and** life-threatening bleeding	any	1 dose, and **consult a Hematologist**

† Consult Table 3 of the Society of Interventional Radiology Consensus Guideline for details *(J Vasc Interv Radiol 2019; 30:1168-84)*

Plasma and Prothrombin Complex Concentrates (PCC; Octaplex®, Beriplex®)

Plasma:

- Plasma transfusion is indicated for prophylaxis against bleeding or for management of acute bleeding in patients with a significant coagulopathy in the setting of multiple coagulation factor deficiencies and when an appropriate coagulation factor concentrate is not available.
- Fresh frozen Plasma (FFP), frozen plasma (FP) and Solvent-Detergent Plasma (SDP), which are all clinically equivalent, and collectively are referred to as Plasma.
    - *Laboratories that stock Plasma in Saskatchewan now predominantly carry SDP.*
- The correct adult dose of plasma is 10-15 mL/kg, which raises coagulation factor levels by approximately 20%.
    - The average volume of 1 unit FFP and FP is 250 mL; SDP is always 200 mL.

      Example: Ordering 10ml/kg of plasma for a 100 kg person would be 4 Units FFP or FP, but 5 units SDP.
    - The duration of efficacy of plasma transfusion is dependent on the factor half-life being replaced.
    - The effectiveness of plasma in reversing an elevated INR is dependent upon the etiology of the coagulopathy.
- Pre-thawed plasma is not routinely stocked by hospitals in Saskatchewan due to storage and thawing equipment requirements.
- A minimum of 30 minutes required for plasma thaw and preparation from the time of product order.

  Request for plasma transfusion in facilities that do not routinely stock plasma or in the outpatient setting may be subject to approval by the on-call Transfusion Medicine Physician.

Prothrombin Complex Concentrates (PCC; Octaplex®, Beriplex®):

- Prothrombin Complex Concentrate (PCC) are lyophilized, viral inactivated/reduced plasma-derived 4-factor concentrates containing coagulation factors II (2), VII (7), IX (9), and X (10); Protein C and S; heparin and sodium citrate. Beriplex® additionally contains human antithrombin and albumin.
- The PCC brands Octaplex® and Beriplex® are considered equivalent in terms of clinical effectiveness.
- Dose must be ordered in International Units (IU), to a maximum dose of 3000 IU.
    - Due to variance in vial sizes, do not order product doses in mL or number of vials.
- **Consultation with a Transfusion Medicine Physician is strongly recommended if use is required for an indication other than warfarin reversal.**
- Indications, as per the National Advisory Committee (NAC) Recommendations for PCC Use in Canada (2022):
    - Emergency reversal of warfarin therapy or severe vitamin K deficiency in patient with an INR 1.5 or greater **and**
        - Life threatening bleeding, or
        - Need for urgent or emergent surgery which cannot be delayed a minimum of 6 hours;

      PCCs are **not** appropriate in a situation where time will allow the INR to return to normal by discontinuing warfarin or through administration of Vitamin K.
- Special considerations include:
    - Emergency management of bleeding in the setting of Factor Xa inhibitor direct oral anticoagulant medications (rivaroxaban (Xarelto®), apixaban (Eliquis®), edoxaban (Lixiana®)) – *off label use*.
    - Massive hemorrhage due to trauma, in the absence of frozen plasma when given concurrently with fibrinogen concentrate – *off label use*.
    - Hypervolemic patients who are coagulopathic and bleeding or pre-procedure, who cannot tolerate plasma.
- Contraindications:
    - Known heparin allergy or history of Heparin Induced Thrombocytopenia (HIT)
    - IgA deficiency with anti-IgA antibodies (applies to Octaplex® only)

- PCC administration is not effective for routine management of:
    - Disseminated Intravascular Coagulopathy (DIC)
    - Liver dysfunction/disease associated coagulopathy
    - Bleeding associated with heparin-based anticoagulants and antiplatelet agents
- Maximum rate of PCC infusion for all indications is 1000 IU over 5 minutes.
    - Consult the SHA PCC Monograph for additional information and administration details.
- In the setting of INR based dosing for warfarin reversal, repeat INR should be drawn as soon as feasible (ideally within 5-30 minutes) following PCC administration to ensure target INR is achieved.

PLASMA TRANSFUSION / PROTHROMBIN COMPLEX CONCENTRATE (PCC) – INPATIENT		
Clinical Setting		**Recommendation and dose**
Diagnosis/Indication	**INR**	
Asymptomatic elevated INR without bleeding (regardless of cause)	Any	No plasma or PCC transfusion
Procedure with a low risk† of bleeding, including: • PICC line placement • Tunneled and untunneled central venous line (CVL) placement or removal • Paracentesis, thoracentesis • Endoscopy without biopsy • Bone marrow aspirate and biopsy	Testing not recommended Any INR is acceptable in the setting of chronic liver disease	No plasma or PCC transfusion
Major procedure with a high risk† of bleeding, including: • Lumbar puncture or spinal procedure with hematoma risk • Arterial intervention • Biliary tract intervention or TIPS procedure • Deep abscess drainage • Urinary tract intervention • Solid organ biopsy	Patients with chronic liver disease: Greater than 2.4 General population: Greater than 1.7 or unknown and cannot wait for result	Plasma 10-15 mL/kg
Major non-neuraxial surgery or surgery with expected blood loss greater than 500 ml	Greater than 1.7 or unknown and cannot wait for result	Plasma 10-15 mL/kg
Acquired multiple factor deficiency (disseminated intravascular coagulation, decompensated acute or chronic liver failure) with active bleeding or prior to a major procedure or surgical intervention with a high risk of bleeding	Greater than 1.7 or unknown and cannot wait for result	Plasma 10-15 mL/kg
Congenital coagulation factor deficiency where a factor concentrate is not available **and** • Life threatening bleeding • Urgent surgical procedure required	Greater than 1.4	**Consult a hematologist**

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<table>
<tr><th colspan="3">PLASMA TRANSFUSION / PROTHROMBIN COMPLEX CONCENTRATE (PCC) – INPATIENT</th></tr>
<tr><th colspan="2">Clinical Setting</th><th rowspan="2">Recommendation and dose</th></tr>
<tr><td>Diagnosis/Indication</td><td>INR</td></tr>
<tr><td>Thrombotic thrombocytopenic purpura (TTP)</td><td>Any</td><td>Pending plasma exchange;
Consult a hematologist</td></tr>
<tr><td>Massive hemorrhage</td><td>Greater than 1.7 or unknown and cannot wait for result</td><td>Plasma 10-15 mL/kg
Included with initial massive transfusion protocol product ratio; further use should be guided by PTT/INR or point-of-care testing (TEG)

If Plasma not available:
PCC 2000 IU + Fibrinogen Concentrate 4 g</td></tr>
<tr><td>Urgent WARFARIN reversal due to
• Non-life-threatening bleeding
• Surgical procedure required in more than 6 hours but less than 5 days</td><td>Greater than 1.7</td><td>No Plasma or PCC
Vitamin K 2-5 mg PO or IV</td></tr>
<tr><td rowspan="3">Emergent WARFARIN reversal due to
• Life threatening bleeding
• Urgent surgical procedure required within 6 hours
Do not use plasma unless PCC is contraindicated
Administer Vitamin K immediately following PCC[#]</td><td>1.5 – 2.9</td><td>PCC 1000 IU + Vitamin K 10 mg IV</td></tr>
<tr><td>3.0 – 5.0
OR unknown and cannot wait for result</td><td>PCC 2000 IU + Vitamin K 10 mg IV</td></tr>
<tr><td>5.1 or greater</td><td>PCC 3000 IU + Vitamin K 10 mg IV</td></tr>
<tr><td>Emergent dabigatran (Pradaxa®) reversal
• Life threatening bleeding
• Urgent surgical procedure required within 6 hours</td><td>Any</td><td>Contact pharmacy for access to idarucizumab (Praxbind®)

If idaracizumab (Praxbind®) not available:
PCC 2000 IU</td></tr>
<tr><td>Emergent reversal of rivaroxaban/Xarelto®, apixaban/Eliquis® or edoxaban/Lixiana®
• Life threatening bleeding
• Urgent surgical procedure required within 6 hours</td><td>Any</td><td>PCC 25-50 units/kg x 1 dose, to a maximum 3000 IU

Transfusion Medicine Physician consultation is strongly recommended</td></tr>
</table>

† Consult Table 3 of the Society of Interventional Radiology Consensus Guideline for details *(J Vasc Interv Radiol 2019; 30:1168-84)*

[#] Vitamin K 10 mg must given by intravenous (IV) route to complete warfarin reversal (do NOT administer by intramuscular or subcutaneous route); PCC effect is only temporary (6 hours) if given alone. Administer Vitamin K immediately following PCC infusion. Onset of action of Vitamin K given IV is approximately 4 hours.

Cryoprecipitate and Fibrinogen Concentrate (FC; RiaSTAP®, Fibryga®)

Cryoprecipitate:

- Cryoprecipitate is an unmodified concentrate of coagulation factor proteins (Factor VIII (8), von Willebrand factor, Factor XIII (13), fibronectin) separated from frozen plasma during a controlled thaw process.
- **Cryoprecipitate use is now limited as it is not pathogen reduced and carries a higher transmissible disease risk compared to fractionated protein concentrates.**
- Cryoprecipitate is indicated for the treatment of bleeding in the setting of acquired or congenital hypofibrinogenemia or congenital Factor XIII (13) deficiency only if factor contentrates are unavailable.
    - Cryoprecipitate is not appropriate for the management of bleeding in patients with Hemophilia A and von Willebrand disease.
- The correct dose of cryoprecipitate for fibrinogen repletion is 1 unit per 10 kg (average 10 units per adult dose).
    - 1 unit cryoprecipitate = 0.285 +/-0.088g fibrinogen (1 SD) or max 5 g of fibrinogen per pool of 10 units.
- Cryoprecipitate must be thawed and issued by the Transfusion Medicine Laboratory as a product pool of 8-10 units per bag (limited inventory available in Saskatoon and Regina only).
- A minimum of 30 minutes required for cryoprecipitate thaw and preparation from the time of product order.

Fibrinogen Concentrate (FC; RiaSTAP®, Fibryga®):

- Fibrinogen Concentrate products contain fibrinogen (1 vial = 0.9-1.3 g)
    - Trace amounts of other substances, such as Factor XIII (13) and fibronectin are not listed as active ingredients and concentrations vary in the final product. Their clinical relevance, if any, is unknown.
- The FC brands RiaSTAP® and Fibryga® are considered equivalent in terms of clinical effectiveness.
- FC is strongly recommended over cryoprecipitate for fibrinogen replacement due to its enhanced safety profile as a lyophilized, virally inactivated product.
- Indications, as per the NAC Statement on Fibrinogen Concentrate Use in Acquired Hypofibrinogenemia (2021):
    - Treatment of bleeding and perioperative prophylaxis in the setting of congenital hypofibrinogenemia;
    - Treatment of bleeding in the setting of acquired hypofibrinogenemia, including massive hemorrhage – *off label, except for the post-surgical setting.*
- Contraindications:
    - Severe allergy to FC.
- Maximum rate of FC infusion in the setting of acquired hypofibrinogenemia is 1 g over 2.5 minutes (4 g over 10 minutes).
    - Consult the SHA Blood Product Monographs for Fibryga or RiaSTAP for additional information and administration details.
- **Consultation with a Transfusion Medicine Physician is strongly recommended to discuss FC dosing.**

FIBRINOGEN CONCENTRATE (FC) AMINISTRATION – INPATIENT		
Clinical Setting		**Recommendation and dose**
Diagnosis/Indication	**Fibrinogen Level (g/L)**	**FC dose**
Acquired hypofibrinogenemia **and** bleeding or pre-operatively in a pregnant or post-partum patient	Less than 2.0	4 g
Acquired hypofibrinogenemia **and** bleeding or pre-operatively in disseminated intravascular coagulation or decompensated liver disease (non-pregnant patient)	Less than 1.5	2-4 g
Chronic liver disease and prior to major procedure with a high risk† of bleeding, including	Less than 1.0	4 g
Massive Hemorrhage Protocol, in the absence of plasma	Less than 1.5 or unknown	4 g + PCC 2000 IU
Factor XIII (13) deficiency, suspected or confirmed, **and** plasma derived or recombinant Factor XIII (13) concentrate is unavailable	N/A	N/A

† Consult Table 3 of the Society of Interventional Radiology Consensus Guideline for details *(J Vasc Interv Radiol 2019; 30:1168-84)*

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