# MEMORANDUM

**TO:** Clinical Care Providers, c/o the Saskatchewan Senior Medical Officer Committee
Transfusions Lab Staff, c/o of the Saskatchewan Transfusion Medicine Working Group

**FROM:** Dr. O. Prokopchuk-Gauk, Northern Saskatchewan Consultant, Transfusion Medicine
Dr. D. Ledingham, Southern Saskatchewan Consultant, Transfusion Medicine

**DATE:** January 11, 2017

**RE:** **Prothrombin Complex Concentrate (PCC) dosing recommendations for emergent warfarin reversal**

Effective immediately, the Saskatchewan Transfusion Medicine Service is recommending a standardized approach to 4-factor PCC dosing for emergent reversal of vitamin K antagonists, including warfarin. Plasma should not be used to manage warfarin-associated coagulopathy with major bleeding, since high-quality evidence demonstrates that the use of PCC is superior to plasma for rapid INR reduction in this setting.[1]

Currently available brands of PCC in Canada include Octaplex® or Beriplex®.[2,3] The only approved indications for PCC use are rapid reversal of warfarin related anticoagulation or vitamin K deficiency with an INR 1.5 or greater in the setting of:

- Major bleeding (life or limb threatening)
- Need for an unplanned surgery *which cannot be delayed for a minimum of 6 hours*

We are recommending that initial **PCC dosing should be based on the INR measured**, as follows:

| | **INR 1.5-2.9** | **INR 3.0-5.0** | **INR 5.1 or greater** |
|---|---|---|---|
| **PCC Dose** | 1000 IU (40 mL) | 2000 IU (80 mL) | 3000 IU (120 mL) |

The dose in International Units (IU) or milliliters (mL) must be indicated upon product order (not the number of vials). A blood sample for INR reassessment should be sent 15 minutes following PCC administration to evaluate for achievement of the target INR of 1.4 or less. If the target INR is not achieved, administration an additional dose of PCC may be considered.

The effect of PCC is short-term, and full warfarin reversal is dependent on concurrent vitamin K administration. The recommended dose of vitamin K for acute warfarin reversal is 10 mg given intravenously.

This dosing strategy is included as a part of the recommendations for PCC use in Canada by the National Advisory Committee on Blood and Blood Products (NAC), and is currently in place in both the Regina Qu'Appelle Health Region and Saskatoon Health Region.

PCC dosing that is INR based only, or INR and weight based, leads to achievement of the target INR of 1.4 or less more reliably than with the fixed dose of 1000 IU.[2,5] There is no known benefit to including the patient weight in PCC calculation over the INR based dosing only.

A reminder, that PCC is a pooled human blood product and consent for blood transfusion must be obtained prior to its infusion. The most significant potential adverse event is that of thrombosis, with an

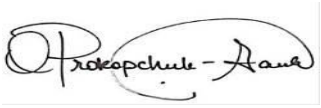
overall rate of at least 1 in 100 patients receiving PCC.[1,3] The risk of allergic reaction or transfusion acquired infection is extremely rare. PCC contains a small amount of heparin, and is contraindicated in patients with known heparin induced thrombocytopenia (HIT).[2,3]

Rural sites that currently do not carry PCC but are interested in stocking this product are eligible for review by the Provincial Transfusion Medicine Service, upon request. Please contact your regional Transfusion Medicine Laboratory for information about local PCC availability.

Details regarding PCC indications and reconstitution may be found on the NAC website at: http://www.nacblood.ca/resources/guidelines/PCC.html.

Please feel free to contact the on-call Transfusion Medicine physician with any questions about PCC use or dosing. Thank you for your attention.

Sincerely,



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**References**

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2. Octaplex Health Canada Product Monograph. <<http://www.octapharma.ca/fileadmin/user_upload/octapharma.ca/20120613_PM_Octaplex_approved.pdf>> Accessed January 6, 2017.
3. Beriplex Health Canada Product Monograph. <<http://labeling.cslbehring.ca/PM/CA/Beriplex-PN/EN/Beriplex-PN-Product-Monograph.pdf>> Accessed January 6, 2017.
4. Abdoellakhan RA, Miah IP, Khorsand N, et al. Fixed Versus Variable Dosing of Prothrombin Complex Concentrate in Vitamin K Antagonist-Related Intracranial Hemorrhage: A Retrospective Analysis. *Neurocrit Care*. Epub ahead of print. 2016. DOI:10.1007/s12028-016-0248-8. Accessed January 6, 2017.
5. Mallik Z, Blain H, Gerges H, et al. Prothrombin complex concentrates – dosing implications. *CSTM 2016 Conference Abstracts*. <<http://www.transfusion.ca/Education/Conference-Abstracts>> Accessed January 6, 2017.