RECOMMENDATIONS FOR USE OF OCTAPLEX® IN CANADA

NATIONAL ADVISORY COMMITTEE ON BLOOD AND BLOOD PRODUCTS RECOMMENDATIONS FOR USE OF OCTAPLEX®

BACKGROUND:

The National Advisory Committee on Blood and Blood Products (NAC) is an interprovincial medical and technical advisory body to the provincial and territorial health ministries and the blood supplier Canadian Blood Services (CBS). Its mandate is to provide professional leadership in assisting in identifying, designing and implementing cost-effective blood utilization management initiatives for the optimization of patient care throughout Canada. In 2008, NAC was approached by the CBS to develop national recommendations for appropriate use and distribution of the prothrombin complex concentrate, octaplex®.

Although prothrombin complex concentrates have been around for many years only recently has a PCC been licensed by Health Canada. This product is produced by Octapharma Canada under the name of octaplex®, and is currently available for distribution through Canadian Blood Services (CBS). Octaplex®is a human plasma derived prothrombin complex concentrate (PCC) that has undergone solvent/detergent treatment and nanofiltration for viral inactivation/removal. This product contains coagulation factors II, VII, IX, X, Protein C, and Protein S - see product composition below. The product monograph states that it is indicated when "rapid correction of prothrombin complex levels is necessary, such as major bleeding or emergency surgery. In other cases, reduction of the dose of the vitamin K antagonist and/or administration of Vitamin K is usually sufficient".

Oral vitamin K antagonists, such as warfarin, are in widespread use for the prevention and treatment of thromboembolic disorders. Bleeding is the most significant adverse event of this therapy occurring with a reported incidence of up to 2.7 major bleeds per 100 patient years. Rapid reversal of the anticoagulation in bleeding patients or prior to urgent surgery is critical in mitigating morbidity and mortality. The therapeutic options to do so include the administration of fresh frozen plasma (FFP) or prothrombin complex concentrates (PCC), with or without concomitant administration of Vitamin K. With the time constraints around administration of FFP, in addition to the risk of hypervolemia, the administration of PCCs with Vitamin K supplementation is the most effective method for rapid reversal of anticoagulation therapy. It however requires careful risk benefit evaluation with an awareness of contraindications and laboratory followup for dose adjustment.

Due to inventory concerns, lack of strong randomized control trial evidence of efficacy and the potential for thrombotic complications, the inventory distribution and use of this product will be limited to facilities that are capable of performing the necessary diagnostic evaluations to ensure that the patient's symptoms are secondary to warfarin overdose and any physicians administering the product may be required to provide justification and outcome reporting to a physician with expertise in thrombosis/hemostasis/transfusion medicine. These caveats will ensure appropriateness of indication, dosing of the product and management of its potential complications. Provincial input as to the facilities that meet these criteria will be required by CBS prior to widespread inventory distribution. Utilization review of this product (indication and outcome) will be undertaken by NAC and/or CBS within the first year of product availability in Canada.

PRODUCT COMPOSITION:

- One 20 mL vial of octaplex® contains the following:

Human Coagulation Factor II	220-760 IU
Human Coagulation Factor VII	180-480 IU
Human Coagulation Factor IX	400-620 IU
Human Coagulation Factor X	360-600 IU
Protein C	140-620 IU
Protein S	140-640 IU
Heparin	80-310 IU
Sodium citrate	17-27 mmol/L

- Reconstituted solution contains approximately 25 IU of prothrombin complex per mL

INDICATIONS:

Recommended in:

A. Reversal of warfarin therapy or vitamin K deficiency in patients exhibiting major bleeding manifestations.

B. Reversal of warfarin therapy or vitamin K deficiency in patients requiring urgent (<6 hour) surgical procedures.

If a study is available all qualified patients should be encouraged to participate in the study rather than receiving open-label product.

Contraindicated in:

A. Patients with a history of Heparin Induced Thrombocytopenia

Not recommended* for:

A. Elective reversal of oral anticoagulant therapy pre – invasive procedure.
B. Treatment of elevated INRs without bleeding or need for surgical intervention. For management of vitamin K antagonist overdose with elevated INR but without bleeding, please refer to the ACCP 2008 recommendations.
C. Massive transfusion
D. Coagulopathy associated with Liver dysfunction
E. Patients with recent history of thrombosis, myocardial infarction, recent ischemic stroke or Disseminated Intravascular Coagulation (DIC)

* There may be extenuating clinical circumstances necessitating use of octaplex® in these clinical situations. They should be evaluated on a case-by-case basis with a physician experienced in the use of this product. Assessment of antithrombin III levels is recommended if the decision to use product in liver dysfunction and DIC patients to ensure that ATIII and/or heparin are not required prior to PCC administration.

Special patient populations:

A. Pregnant and lactating women – there is insufficient evidence available to allow a recommendation for use of this product in this patient population. Caution should be exercised if used in pregnancy, particularly in the peripartum/early postpartum period because of heightened tendency to thrombosis.

B. Pediatric patients – there is insufficient evidence available to allow a recommendation for use of this product in this patient population.
C. Congenital factor II or X deficient patients – use of the product should be at the discretion of the local Hemophilia clinic.

DOSING, ADMINISTRATION & MONITORING:
The following recommendation is based on review of literature and the desire to prevent thrombotic complications. The subcommittee is aware that it may be less than the manufacturer's recommended dose in many individuals.

For adult patients:

40 mL octaplex® (1000 IU Factor IX activity*) **and** 10 mg Vitamin K IV

*A higher or second dose may be needed in extremes of INR or weight, suggest consultation with a specialist in hematology or transfusion medicine in these situations.

Maximum total dose: **120 mL or 3000 IU Factor IX activity.**

Administration: Must be administered intravenously.
The rate of infusion should not exceed 2- 3mL/min.

Post dose monitoring: INR – 10-15 minutes
Clinical outcomes (incl. thrombotic events) – 24 hour and 30 day

REFERENCES

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