

March 25, 2008

Dear Healthcare Professional:

**Re: Availability of octaplex®**

Octapharma Canada Inc. is pleased to inform you that octaplex® will be available through Canadian Blood Services from May 2008.

octaplex® (Human Prothrombin Complex – Human Coagulation Factor II, VII, IX and X in combination) is Octapharma's unique prothrombin complex concentrate (PCC), currently licensed in 26 countries worldwide for the treatment and prophylaxis of bleeding in hereditary and/or acquired coagulation deficiencies of the prothrombin complex factors. In Canada, octaplex® is approved for the treatment and perioperative prophylaxis of bleeding in acquired deficiency of the prothrombin complex coagulation factors, such as deficiency caused by treatment with vitamin K antagonists, or in case of overdose of vitamin K antagonists, when rapid correction of the deficiency is required<sup>1</sup>.

Since octaplex® received its first licence, more than 146,000,000 units have been infused in approximately 49,000 patients worldwide. The well-balanced proportion of coagulation factors (II, VII, IX and X) and therapeutic concentrations of proteins C and S make octaplex® a highly effective and tolerable PCC<sup>2</sup>. In addition, octaplex® has a fast onset of action (less than 10 minutes)<sup>3</sup> – this is especially useful for the rapid reversal of anticoagulants in bleeding patients or prior to urgent surgery, and the rapid correction of bleeding due to vitamin K deficiencies.

**Highly effective and tolerable:** In octaplex®, the activities of the four vitamin-K dependent clotting factors II, VII, IX and X are in ratios of approx. 1:1:1:1<sup>4</sup>. The inhibitor proteins C and S are also present in therapeutically effective concentrations, and the content of activated FVII is low with a ratio of FVII to FVIIa activity of at least 5:1 – this minimises the risk of thrombogenicity<sup>5</sup>. In a recently published clinical trial of patients requiring immediate reversal of oral anticoagulation, 60 patients received a median total octaplex® dose of 41.1 (15.3–83.3) IU/kg body weight; of the 56 patients evaluable in terms of efficacy,

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<sup>1</sup> octaplex® Product Monograph, dated 29 November 2007.

<sup>2</sup> Josic, D. et al, Manufacturing of a prothrombin complex concentrate aiming at low thrombogenicity. Thrombosis Research 2000; 100: 433-441.

<sup>3</sup> Riess, H. et al, Prothrombin complex concentrate (octaplex®) in patients requiring immediate reversal of oral anticoagulation. Thrombosis Research, 2007; 1: 9-16.

<sup>4</sup> Josic, D. et al, Manufacturing of a prothrombin complex concentrate aiming at low thrombogenicity. Thrombosis Research 2000; 100: 433-441.

<sup>5</sup> Josic, D. et al, Manufacturing of a prothrombin complex concentrate aiming at low thrombogenicity. Thrombosis Research 2000; 100: 433-441.

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51 (91%) responded and their control of bleedings was rated as ‘excellent’ by the investigators<sup>6</sup>. No thrombotic side effects were observed<sup>7</sup>.

**Fast onset of action:** Bleeding is the most serious adverse event of oral anticoagulants and is a major cause of mortality in such patients. Rapid reversal of anticoagulation in bleeding patients or prior to urgent surgery is mandatory. In the recent octaplex<sup>®</sup> clinical trial, the median INR of patients declined from 2.8 (1.5–9.5) to 1.1 (1.0–1.9) within 10 minutes; the INR for 93% of the 56 evaluable patients decreased to a value below 1.4 within one hour after dosing<sup>8</sup>.

**Product information:** octaplex<sup>®</sup> is available in one presentation size – 500IU FIX reconstituted with 20 mL of Water for Injection. Each octaplex<sup>®</sup> product kit includes a Mix2Vial™ transfer set for quick and easy reconstitution of the lyophilised product.

octaplex<sup>®</sup> is room temperature approved, thereby allowing for convenient storage and access in the ER.

If you have any questions or require additional information on octaplex<sup>®</sup> (e.g. copy of the product monograph), please contact Octapharma Canada at [anu.bhucher@octapharma.ca](mailto:anu.bhucher@octapharma.ca) or 1-416-531-5533.

Sincerely,

Anu Bhucher  
Octapharma Canada Inc

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<sup>6</sup> Riess, H. et al, Prothrombin complex concentrate (octaplex<sup>®</sup>) in patients requiring immediate reversal of oral anticoagulation. Thrombosis Research, 2007; 1: 9-16.

<sup>7</sup> Riess, H. et al, Prothrombin complex concentrate (octaplex<sup>®</sup>) in patients requiring immediate reversal of oral anticoagulation. Thrombosis Research, 2007; 1: 9-16.

<sup>8</sup> Riess, H. et al, Prothrombin complex concentrate (octaplex<sup>®</sup>) in patients requiring immediate reversal of oral anticoagulation. Thrombosis Research, 2007; 1: 9-16.