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 required1.

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 PCC2. In addition, octaplex® has a fast onset of action (less than 10 minutes)3 – 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. 1:1:1:4. 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 thrombogenicity4. 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,

1 octaplex® Product Monograph, dated 29 November 2007.
51 (91%) responded and their control of bleedings was rated as ‘excellent’ by the investigators\textsuperscript{6}. No thrombotic side effects were observed\textsuperscript{7}.

\textbf{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\textsuperscript{5} 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\textsuperscript{8}.

\textbf{Product information}: octaplex\textsuperscript{5} is available in one presentation size – 500IU FIX reconstituted with 20 mL of Water for Injection. Each octaplex\textsuperscript{5} product kit includes a Mix2Vial\textsuperscript{TM} transfer set for quick and easy reconstitution of the lyophilised product.

octaplex\textsuperscript{5} 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\textsuperscript{5} (e.g. copy of the product monograph), please contact Octapharma Canada at anu.blucher@octapharma.ca or 1-416-531-5533.

Sincerely,

Anu Bhucher
Octapharma Canada Inc

\textsuperscript{6} Riess, H. et al, Prothrombin complex concentrate (octaplex\textsuperscript{5}) in patients requiring immediate reversal of oral anticoagulation. Thrombosis Research, 2007; 1: 9-16.
\textsuperscript{7} Riess, H. et al, Prothrombin complex concentrate (octaplex\textsuperscript{5}) in patients requiring immediate reversal of oral anticoagulation. Thrombosis Research, 2007; 1: 9-16.
\textsuperscript{8} Riess, H. et al, Prothrombin complex concentrate (octaplex\textsuperscript{5}) in patients requiring immediate reversal of oral anticoagulation. Thrombosis Research, 2007; 1: 9-16.