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March 7th, 2018

Subject: **PrAdynovate™ [Antihemophilic Factor (Recombinant), PEGylated], the full-length form of PrAdvate®, now pegylated to provide a true extended-half life (EHL) Factor VIII product, is now available through the Canadian Blood Services (CBS)**

Dear Healthcare Professional,

Shire Canada is delighted to notify you of the availability of PrAdynovate. This latest hematology innovation from Shire, is a pegylated recombinant Antihemophilic factor form of the PrAdvate legacy, standard half-life product. Pr Adynovate is indicated in patients (≥12 years) with hemophilia A (congenital factor VIII deficiency) for the following indications:

1. Control and prevention of bleeding episodes
2. Prophylaxis to prevent or reduce the frequency of bleeding episodes
3. Perioperative management

PrAdynovate is now available for order through Canadian Blood Services (CBS). PrAdynovate received Health Canada approval on November 17, 2016 and **will now be the only EHL product available through the Canadian Blood Services** for patients ≥ 12 years old or patients not currently on Immune Tolerance Induction (ITI) therapy with another EHL product.

The terminal plasma half-life of PrAdynovate is 1.4- to 1.5-fold, longer than that of PrAdvate. Because PrAdynovate is a true extended-half life, rFVIII, patients can decrease their infusions to twice weekly with PrAdynovate for prophylaxis therapy.

The safety, efficacy, and pharmacokinetics (PK) of PrAdynovate were evaluated in a multicenter, open label, prospective, non-randomized, two-arm clinical study that assessed the efficacy of a twice weekly prophylactic treatment regimen, assessed the efficacy of on-demand treatment, and determined hemostatic efficacy in the treatment of bleeding episodes. Prophylaxis with PrAdynovate resulted in an Annual Bleed Rate (ABR) that was significantly lower than half the ABR of on-demand treatment ($P < .0001$). The median ABR was 1.9, and 39.6% of compliant subjects had no bleeding episodes during prophylaxis, whereas subjects treated on demand had a median ABR of 41.5. PrAdynovate was also efficacious for the treatment of bleeding episodes, with 95.9% of bleeding episodes treated with 1 to 2 infusions and 96.1% having efficacy ratings of excellent/good. No FVIII inhibitory antibodies or safety signals were identified. (Konkle et al., *Blood* 2015: 126(9):1078-85.)

PrAdynovate is available in 250, 500, 1000 and 2000 IU/vial lyophilized powder for intravenous injection. Each strength is supplied with 5mL sterile water for injection (USP, Ph.Eur.) for reconstitution and the BAXJECT II Hi-Flow device. Additionally a separate carton containing the following is also provided along with the product carton:

- 1 infusion set
- 1 10 ml sterile syringe
- 2 sterile alcohol swabs
- 2 bandages

PrAdynovate should be stored at refrigerated temperature; 2°to 8°C (36°to 46°F) in powder form. PrAdynovate is contraindicated in patients who have had prior anaphylactic reaction to PrAdynovate, to the parent molecule (PrAdvate), mouse or hamster protein, or excipients of PrAdynovate (Tris, calcium

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chloride, mannitol, sodium chloride, trehalose, glutathione, histidine, and/or polysorbate 80). For a complete listing, see the Dosage Forms, Composition and Packaging section of the Product Monograph.

For additional information, please contact our medical information by email: medinfoca@shire.com or phone: 1-800-268-2772. Please consult the [Pr]Adynovate Product Monograph at https://www.shirecanada.com/-/media/shire/shireglobal/shirecanada/pdffiles/product%20information/Adynovate-pm-en.pdf for important information relating to conditions of clinical use, adverse reactions, drug interactions, dosing instructions, and relevant warnings and precautions regarding: inhibitory antibodies to [Pr]Adynovate; use in pregnant and nursing women; use in paediatrics and geriatrics; and monitoring and laboratory testing.

Yours sincerely,

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Interim Regional Medical Head
Shire Pharma Canada ULC