Subject: Introducing Jivi® – a new recombinant FVIII with an extended half-life from the makers of Kovaltry®

Dear Healthcare Professional,

Bayer is pleased to announce that Jivi®, a new extended half-life (EHL) recombinant Factor VIII (FVIII) treatment for hemophilia A, will be available through Canadian Blood Services (CBS) under the Named Patient Program. Jivi® will be available beginning the week of March 30th, 2020 for vial size 1000 IU, 2000 IU and 3000 IU, while vial size 500 IU will be available in April 2020.

Jivi® is a recombinant B-domain deleted (BDD) human coagulation FVIII variant, which is site-specifically conjugated with a 60 kDa branched polyethylene glycol (PEG) polymer. It is expressed in a baby hamster kidney (BHK) cell line, which is the host cell line used for the licensed Bayer recombinant FVIII products Kogenate® FS and Kovaltry®.[1] The cell culture, PEGylation, purification, and formulation processes used in the manufacture of Jivi® do not use any additives of human or animal origins. In addition, a 20 nm viral filtration step is used to remove process- and product-related impurities.[1]

The site-specific PEGylation of Jivi® results in a molecule which retains full biological coagulant activity. The PEGylation within the A3 domain reduces clearance of FVIII, thereby resulting in an extended half-life and increased area under the concentration-time curve (AUC).[1] Compared with Kogenate® FS, Jivi® had a reduced clearance that resulted in a ~1.4-fold increase in half-life based on CS assay (18.6 h vs. 13.3 h) and dose normalized AUC.[2]

Jivi® (Antihemophilic Factor [Recombinant, B-domain deleted, PEGlylated]) is indicated for use in previously treated adults and adolescents (≥12 years of age) with hemophilia A (congenital FVIII deficiency) for:

- Routine prophylactic treatment to prevent or reduce the frequency of bleeding episodes
- Control and prevention of episodic bleeding
- Peri-operative management of bleeding (surgical prophylaxis)

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Jivi® does not contain von Willebrand factor and is not indicated for the treatment of von Willebrand disease. Safety and efficacy for previously untreated patients (PUPs) have not been studied.

The usual single dose for on-demand treatment of minor to moderate bleeding episodes is 10 to 30 IU/kg repeated every 24-48 hours, with higher dosages recommended for major hemorrhages. The recommended initial dosing regimen for routine prophylaxis is 30 to 40 IU/kg twice weekly. Based on the bleeding episodes, the dosing regimen may be adjusted to 45 to 60 IU/kg every 5 days. A dosing regimen may be further individually adjusted to more or less frequent dosing.

Jivi® is contraindicated in patients who have had prior anaphylactic reactions to this drug or its components, or to mouse or hamster protein. The most frequently reported (≥5%) adverse reactions in clinical trials in PTPs (≥12 years of age) were headache (14.2%), pyrexia (5.4%), nausea (5.4%) and cough (6.8%). In addition, a clinical immune response associated with anti-PEG antibodies, manifested as symptoms of acute hypersensitivity and/or loss of drug effect has been observed, in the first 4 EDs, primarily in patients <6 years of age. No *de novo* or confirmed cases of inhibitor against FVIII occurred in the clinical study program. A single unconfirmed positive result of a low titre of Factor VIII inhibitor (1.7 BU/mL) was reported in one adult patient following a surgery.

Jivi® is available as a lyophilized powder in single-use glass vials, one vial per carton. It is supplied with a sterile vial adapter with a 15-micrometer filter and a prefilled diluent glass barrel syringe, which together serve as a needleless reconstitution system. The prefilled diluent syringe contains 2.5 mL Sterile Water for Injection, USP for all nominal dose strengths (500 IU, 1000 IU, 2000 IU and 3000 IU). The Nipro SafeTouch™ Winged Infusion set is also provided in the package.

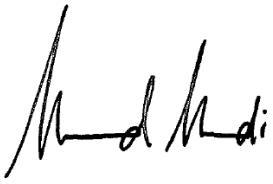
Jivi® should be stored under refrigeration (2 °C – 8 °C). Do NOT freeze. Keep the vial and the pre-filled syringe in the outer carton in order to protect from light. Storage of the lyophilized powder may be done at room temperature (up to 25 °C) for a single period of up to 6 months or up to 30 °C for 3 months. Once the product is removed from refrigeration, it cannot be returned to the refrigerator. The product should be used immediately and no longer than 3 hours after reconstitution.

You can obtain additional information on Jivi® by:

Contacting you local Business Relations Manager or Bayer Medical Information at 1-800-265-7382

Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (http://hc-sc.gc.ca/index-eng.php); the manufacturer's website http://www.bayer.ca or by calling Bayer Medical Information at 1-800-265-7382 or canada.medinfo@bayer.com.

Sincerely,



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References:

1. Mei et al. *Rational design of a fully active, long-acting PEGylated factor VIII for the Treatment of Hemophilia A.* Blood, 15 July 2010, volume 116, Number 2, pages 270 - 279.
2. Jivi Product Monograph, Bayer Inc. October 19, 2018