

**About ELOCTATE: Extending the Interval Between Prophylactic Infusions**

**ELOCTATE™** [Antihemophilic Factor (Recombinant), Fc Fusion Protein] is a recombinant factor VIII therapy approved in the United States for the control and prevention of bleeding episodes, perioperative (surgical) management and routine prophylaxis (protection) in adults and children with hemophilia A. ELOCTATE is not indicated for the treatment of a bleeding disorder called von Willebrand disease. This is the first regulatory approval for ELOCTATE worldwide and the first significant hemophilia A treatment advance in more than two decades. ELOCTATE is the only therapy with prolonged circulation in the body, and the first to reduce the frequency of bleeding episodes with prophylactic infusions every three to five days. The therapy offers people with hemophilia A the potential to extend the interval between prophylactic (protective) infusions.

The recommended starting prophylactic regimen for ELOCTATE is 50 IU/kg every four days. Based on clinical response, the regimen may be adjusted in the range of 25 to 65 IU/kg and every three to five days.

ELOCTATE was developed by fusing B-domain deleted factor VIII to the Fc portion of immunoglobulin G subclass 1, or IgG<sub>1</sub> (a protein commonly found in the body). It is believed that this enables ELOCTATE to use a naturally occurring pathway to prolong the time the therapy remains in the body. While Fc fusion has been used to develop medicines for more than 15 years, Biogen Idec is the only company to apply it to the treatment of hemophilia.

**Clinical Profile**

In the Phase 3 A-LONG study, one of the largest pivotal studies in hemophilia A ever completed (involving 165 participants), ELOCTATE was found to be safe and effective in:

- The control and prevention of bleeding episodes
- Perioperative management
- Routine prophylaxis

The study evaluated individualized and weekly prophylaxis to reduce or prevent bleeding episodes, on-demand therapy to control bleeding when it occurs, and perioperative management. In the individualized prophylaxis arm, participants started on a twice-weekly dosing regimen, which could be adjusted to every three to five days.

The overall median annualized bleeding rate (ABR), or projected number of bleeding episodes per year, reported in the study was 1.6 in the individualized prophylaxis arm, with spontaneous and joint bleeding ABRs both 0.0. In the weekly prophylaxis arm, the overall median ABR was 3.6, with spontaneous and joint bleeding ABRs both 1.9. Study participants achieved a statistically significant reduction of bleeding episodes in each of the study's prophylaxis arms relative to the on-demand treatment arm.

In the Phase 3 study, ELOCTATE demonstrated a prolonged half-life (a measure of the time therapy remains in the body). Factor levels remained above 1 percent – a recommended therapy target set by the National Hemophilia Foundation (NHF) – for approximately five days after a single 50 IU/kg dose of ELOCTATE. Additionally, 98 percent of bleeding episodes were controlled with one or two ELOCTATE infusions.

ELOCTATE was generally well tolerated in the study. No participants in the A-LONG study developed inhibitors to ELOCTATE. One participant had a transient, positive neutralizing antibody test result, which was not

confirmed upon repeat testing. Additionally, no events involving serious allergic reactions or serious vascular (blood) clots were reported in any study participant.

Across routine prophylaxis and on-demand therapy arms, adverse reactions were reported in 5.5 percent of participants. Common adverse reactions (incidence greater than or equal to 1 percent) were arthralgia (joint pain) and malaise (general discomfort), which were each reported in two study participants. Two participants were withdrawn from the study due to adverse reactions: one participant due to rash and one due to arthralgia.

The pediatric indication for ELOCTATE is supported by interim results from 38 boys two to 11 years of age from the Kids A-LONG study. These data showed that ELOCTATE was generally well tolerated and no inhibitors were detected. The relative increase in half-life seen with ELOCTATE was consistent with findings in adults and adolescents. In April 2014, Biogen Idec and Swedish Orphan Biovitrum (Sobi) reported positive top-line results for the completed Kids A-LONG study, which confirmed and expanded upon the interim data.

Biogen Idec is currently conducting ASPIRE, an extension study to evaluate ELOCTATE's long-term safety and efficacy.

#### **About Hemophilia A**

Hemophilia A is a rare, chronic, genetic disorder in which blood clot formation is impaired. It is caused by having substantially reduced or no factor VIII activity, which is needed for normal blood clotting. Hemophilia A occurs in about one in 5,000 male births annually, and more rarely in females.<sup>1</sup> Approximately 16,000 people in the United States have hemophilia A. According to the World Federation of Hemophilia, an estimated 400,000 people are living with hemophilia, but only about 142,000 people are currently diagnosed with hemophilia A worldwide.<sup>2</sup> People with hemophilia A experience prolonged bleeding episodes that may cause pain, irreversible joint damage and life-threatening hemorrhages.

Prophylactic infusions of factor VIII can temporarily replace the missing clotting factor that is needed to control bleeding and prevent new bleeding episodes. The NHF recommends routine prophylaxis as optimal for the treatment of people with severe hemophilia A. In recent years, regimens have shifted from on-demand treatment to routine prophylaxis because of observed improvement in long-term clinical outcomes, such as joint damage. According to NHF guidelines, traditional prophylactic hemophilia A therapy involves infusions three times per week or every other day, which equates to approximately 150 to 180 infusions per year.

#### **ELOCTATE: U.S. Approval and Global Regulatory Status**

ELOCTATE was approved in the United States in June 2014 for the control and prevention of bleeding episodes, perioperative management and routine prophylaxis in adults and children with hemophilia A. ELOCTATE is not indicated for the treatment of a bleeding disorder called von Willebrand disease.

Regulatory applications for ELOCTATE are currently under review in several countries including Canada, Australia and Japan.

Biogen Idec and Swedish Orphan Biovitrum (Sobi) are collaborators in the development and commercialization of ELOCTATE for hemophilia A. Biogen Idec leads development, has manufacturing rights, and has commercialization rights in North America and all other regions excluding the Sobi territory. Sobi has the right

to opt in to assume final development and commercialization rights in Europe, Russia, the Middle East and Northern Africa.

### Important Safety Information

Do not use ELOCTATE if you have had an allergic reaction to it in the past.

Tell your healthcare provider if you have or have had any medical problems, take any medicines, including prescription and non-prescription medicines, supplements, or herbal medicines, have any allergies, are breastfeeding, are pregnant or planning to become pregnant, or have been told you have inhibitors (antibodies) to Factor VIII.

Allergic reactions may occur with ELOCTATE. Call your healthcare provider or get emergency treatment right away if you have any of the following symptoms: difficulty breathing, chest tightness, swelling of the face, rash, or hives.

Your body can also make antibodies called, “inhibitors,” against ELOCTATE, which may stop ELOCTATE from working properly.

Common side effects of ELOCTATE are joint pain and general discomfort. These are not all the possible side effects of ELOCTATE. Talk to your healthcare provider right away about any side effect that bothers you or that does not go away, and if bleeding is not controlled after using ELOCTATE.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit [www.fda.gov/medwatch](http://www.fda.gov/medwatch), or call 1-800-FDA-1088.

Please see [www.ELOCTATE.com](http://www.ELOCTATE.com) for full Prescribing Information.

For more information on ELOCTATE clinical studies, visit [www.ELOCTATE.com](http://www.ELOCTATE.com) or [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov).

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<sup>1</sup> National Hemophilia Foundation. Hemophilia A (Factor VIII Deficiency). <http://www.hemophilia.org/NHFWeb/MainPgs/MainNHF.aspx?menuid=180&contentid=45&rptname=bleeding>. Accessed January 28, 2014.

<sup>2</sup> World Federation of Hemophilia. Annual Global Survey 2012. <http://www1.wfh.org/publications/files/pdf-1574.pdf>. Accessed January 28, 2014.