Altuviiio™ (antihemophilic factor [recombinant], Fc-VWF-XTEN fusion protein-ehtl) – New orphan drug approval

- On February 22, 2023, the FDA approved Bioverativ Therapeutics and Sanofi's Altuviiio (antihemophilic factor [recombinant], Fc-VWF-XTEN fusion protein-ehtl), for use in adults and children with hemophilia A (congenital factor VIII deficiency) for:
    - Routine prophylaxis to reduce the frequency of bleeding episodes
    - On-demand treatment and control of bleeding episodes
    - Perioperative management of bleeding.
- Altuviiio is not indicated for the treatment of von Willebrand disease.
- Altuviiio is a von Willebrand Factor independent recombinant DNA-derived, Factor VIII (FVIII) concentrate.
- The efficacy of Altuviiio as routine prophylaxis was established in an open-label study in adult and adolescents with severe hemophilia A. A total of 133 adults and adolescents, who were on pre-study FVIII prophylaxis, were assigned to receive Altuviiio for routine prophylaxis for 52 weeks (Arm A). An additional 26 patients, who were on pre-study episodic (on-demand) treatment with FVIII, received episodic (on-demand) treatment with Altuviiio for 26 weeks, followed by routine prophylaxis for 26 weeks (Arm B). The efficacy was evaluated as estimated by the mean annualized bleed rate (ABR) and by comparing the ABR during on-study prophylaxis vs. the ABR during pre-study FVIII prophylaxis.

	Arm A Prophylaxis	Arm B On-demand	Arm B Prophylaxis
Treated bleeds			
Mean ABR (95% CI)	0.7 (0.5, 1.0)	21.4 (18.8, 24.4)	0.7 (0.3, 1.5)
Median ABR (Q1, Q3)	0 (0, 1.0)	21.1 (15.1, 27.1)	0 (0, 0)
Subjects with zero bleeds, n (%)	82 (64.1)	0	20 (76.9)

    - An intra-subject comparison (N = 78) between mean ABR during on-study prophylaxis with Altuviiio and that during pre-study FVIII prophylaxis yielded a 77% reduction in treated bleeds (95% CI: 58, 87).
- In addition, the efficacy of Altuviiio as routine prophylaxis in 67 children < 12 years was estimated by the mean ABR. In patients with at least 26 weeks of exposure, routine prophylaxis resulted in a mean ABR of 0.5 (95% CI: 0.2, 1.3) and a median ABR of 0 (Q1, Q3: 0, 1.3) for treated bleeds.
- The efficacy of Altuviiio in control of bleeds was evaluated in the adult and adolescent study, with a total of 362 bleeding episodes being treated with Altuviiio (most occurring during on-demand treatment in Arm B). Response to the first injection was assessed by patients at least 8 hours after treatment. A 4-point rating scale of excellent, good, moderate, and no response was used to assess response. Bleeding was resolved with a single injection of Altuviiio in 96.7% of bleeding episodes.
- For perioperative management of bleeding, the efficacy of Altuviiio was assessed in 13 major surgeries in 12 patients (11 adults and 1 child). The clinical evaluation of hemostatic response during major surgery was assessed using a 4-point scale of excellent, good, moderate, or

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poor/none. The hemostatic effect of Altuviiio was rated as “excellent” in 13 of 13 surgeries (100%). Perioperative hemostasis was also assessed in 22 minor surgeries in 19 patients (12 adults and 7 children). The hemostatic response was evaluated by the investigator/surgeon in 15 of these minor surgeries; an excellent response was reported in all (100%).

- Warnings and precautions for Altuviiio include hypersensitivity reactions, neutralizing antibodies, monitoring laboratory tests.
- The most common adverse reactions (> 10%) with Altuviiio use were headache and arthralgia.
- The recommended dosing for Altuviiio for routine prophylaxis for adults and children is 50 IU/kg administered intravenously once weekly.
- Refer to the Altuviiio drug label for dosing for on-demand treatment and perioperative management.
- Sanofi’s launch plans for Altuviiio are pending. Altuviiio will be available as 250, 500, 750, 1000, 2000, 3000, or 4000 IU lyophilized powder in single-dose vials for reconstitution.

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