

Roctavian™ (valoctocogene roxaparvovec-rvox)

When requesting Roctavian™ (valoctocogene roxaparvovec-rvox), the individual requiring treatment must be diagnosed with the following FDA-approved indication and meet the specific coverage guidelines and applicable safety criteria for the covered indication.

FDA-Approved Indication

Roctavian is an adeno-associated virus vector-based gene therapy indicated for the treatment of adults with severe hemophilia A (congenital factor VIII deficiency with factor VIII activity < 1 IU/dL) without antibodies to adeno-associated virus serotype 5 (AAV5) detected by an FDA-approved test.

Coverage Guidelines

Hemophilia A

The individual must meet all of the following criteria for authorization:

- Is male;
- Is 18 years of age or older;
- Has severe hemophilia A as evidence by a baseline (without Factor VIII replacement therapy) Factor VIII level of < 1 IU/dL;
- Does not have detectable pre-existing antibodies to adeno-associated virus 5 (AAV5) by an FDA-approved test;
- Has a history of use of Factor VIII therapy for at least 150 exposure days;
- Performed Factor VIII inhibitor titer testing within 30 days before intended receipt of Roctavian;
- Does not currently have an inhibitor to Factor VIII;
- Does not have a history of Factor VIII inhibitors;
- Prophylactic therapy with Factor VIII will not be given after Roctavian administration once adequate Factor VIII levels have been achieved (*Note: use of episodic Factor VIII therapy is acceptable for the treatment of bleeds and for surgery/procedures if needed*);
- Has not received Roctavian in the past;
- Does not have a known hypersensitivity to mannitol;
- Does not have an active acute or uncontrolled chronic infection;
- Does not have chronic or active hepatitis B;
- Does not have active hepatitis C;

- Does not have evidence of significant hepatic fibrosis or cirrhosis;
- Has undergone a liver health assessment within 30 days before intended receipt of Roctavian and meets all of the following (*Note: if one or more of the laboratory values listed below is not at the value specified below, the individual has been evaluated and determined that the use of Roctavian is clinically appropriate by a hepatologist*):
 - o Alanine aminotransferase levels are $\leq 1.25 \times$ the upper limit of normal (ULN);
 - o Aspartate aminotransferase levels are $\leq 1.25 \times$ ULN;
 - o Total bilirubin levels are $\leq 1.25 \times$ ULN;
 - o Alkaline phosphatase levels are $\leq 1.25 \times$ ULN;
 - o Gamma-glutamyl transferase levels are $\leq 1.25 \times$ ULN;
 - o International Normalization ratio is < 1.4
- The platelet count was $\geq 100 \times 10^9/L$ within 30 days before intended receipt of Roctavian;
- The creatinine level was < 1.4 mg/dL within 30 days before intended receipt of Roctavian;
- Has not used a systemic immunosuppressive agent within 30 days before intended receipt of Roctavian (*Note: corticosteroids are not included as systemic immunosuppressive agents*);
- Does not have any disease or condition that would interfere with the compliance requirement that involve use of systemic corticosteroid therapy or systemic alternative immunosuppressive medications;
- Does not have an immunosuppressive disorder;
- Is not human immunodeficiency virus positive;
- Does not have any additional bleeding disorder, besides Hemophilia A;
- Does not have a history of thrombosis or thrombophilia;
- Does not have a current active malignancy (*Note: current active malignancy does not include non-melanoma skin cancer*);
- Does not have a history of hepatic malignancy;
- Has not received a live vaccine within 30 days before intended receipt of Roctavian;
- The following precautions have been discussed with the patient by a hemophilia specialist physician;
 - o A male of reproductive potential (and his female partner) should prevent or postpone pregnancy by utilizing an effective form of contraception for a period of up to 6 months after administration of Roctavian; AND
 - o A male should not donate semen for a period of up to 6 months after administration of Roctavian;
- Current body weight has been obtained within 30 days before intended receipt of Roctavian;
- Roctavian is prescribed by a hemophilia specialist physician.

Approval duration: One time (per lifetime)

Dosing Recommendation

Roctavian is for one-time single-dose intravenous use only.

The recommended dose of Roctavian is 6×10^{13} vector genomes (vg) per kg of body weight.

References

1. Roctavian® intravenous infusion [prescribing information]. Novato, CA: BioMarin; June 2023.
2. Peyvandi F, Garagiola I, Young G. The past and future of haemophilia: diagnosis, treatments and its complications. *Lancet*. 2016;388(10040):187-197.
3. Centers for Disease Control and Prevention. Community Counts: Hemophilia Home Page. Lasted reviewed in July 2023. Available at: <https://www.cdc.gov/ncbddd/hemophilia/facts.html>. Accessed on August 14, 2023.
4. Mancuso ME, Mahlangu JN, Pipe SW. The changing treatment landscape in haemophilia: from standard half-life clotting Factor concentrates to gene editing. *Lancet*. 2021;397:630-640.
5. Croteau SE. Hemophilia A/B. *Hematol Oncol Clin North Am*. 2022;36(4):797-812.
6. Franchini M, Mannucci PM. The more recent history of hemophilia treatment. *Semin Thromb Hemost*. 2022;48(8):904-910.
7. National Hemophilia Foundation. MASAC (Medical and Scientific Advisory Council) recommendations concerning products licensed for the treatment of hemophilia and other selected disorders of the coagulation system (endorsed by the National Hemophilia Foundation Board of Directors on May 2, 2023). MASAC Document #276. Available at: <https://www.hemophilia.org/sites/default/files/document/files/MASACTreatment.pdf>. Accessed on August 13, 2023.
8. Ozelo MC, Mahlangu J, Pasi KJ, et al, for the GENE8-1 trial group. Valoctocogene roxaparvovec gene therapy for hemophilia A. *N Engl J Med*. 2022;386(11):1013-1025.
9. Mahlangu J, Kaczmarek R, Von Drygalski A, et al, for the GENE8-1 trial group. Two-year outcomes of valoctocogene roxaparvovec therapy for hemophilia A. *N Engl J Med*. 2023;388(8):694-705.