Clinical Policy: Valoctocogene Roxaparvovec-rvox (Roctavian)

Reference Number: PA.CP.PHAR.466
Effective Date: 08/2023
Last Review Date: 01/2024

Description
Valoctocogene roxaparvovec-rvox (Roctavian™) is adeno-associated virus (AAV) vector-based gene therapy.

FDA Approved Indication(s)
Valoctocogene roxaparvovec-rvox is indicated for the treatment of adults with severe hemophilia A (congenital factor VIII [FVIII] deficiency with FVIII activity < 1 IU/dL) without pre-existing antibodies to adeno-associated virus serotype 5 (AAV5) detected by an FDA-approved test.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Roctavian is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Congenital Hemophilia A (must meet all)**:**

1. Diagnosis of congenital hemophilia A;
2. Prescribed by or in consultation with a hematologist;
3. Age ≥ 18 years;
4. Member has severe hemophilia A (defined as pre-treatment FVIII level < 1% or activity < 1 IU/dL);
5. Member has been adherent with use of a FVIII product* for routine prophylaxis for at least 12 months as assessed and documented by provider;
   **Prior authorization may be required*
6. Member has been treated with FVIII concentrates or cryoprecipitate for a minimum of 150 exposure days (EDs);
7. Member meets both of the following (a and b):
   a. No previous documented history of a detectable FVIII inhibitor;
   b. Member has FVIII inhibitor level assay < 0.6 Bethesda units (BU) on 2 consecutive occasions at least one week apart within the last 12 months;
8. Member has no pre-existing antibodies to AAV5 as measured by an FDA-approved test;
9. Documentation of hepatic ultrasound and elastography or laboratory assessments for liver fibrosis within the last 3 months showing there is not significant hepatic fibrosis (stage 3 or 4) or cirrhosis;
10. Attestation from hepatologist that member is eligible for Roctavian if any of the following (a, b, or c) baseline liver abnormalities, assessed within the last 3 months, are present:
    a. Radiological liver abnormalities;

b. Liver function tests (LFTs) (i.e., alanine aminotransferase [ALT], aspartate aminotransferase [AST], gamma-glutamyl transferase [GGT], alkaline phosphatase [ALP], total bilirubin) measuring ALT, AST, GGT, ALP and total bilirubin > 1.25 × upper limit of normal (ULN);
c. International normalized ratio (INR) ≥ 1.4;

11. Provider attestation of member's ability to receive corticosteroids and/or other immunosuppressive therapy that may be required for an extended period and that the risks associated with immunosuppression are acceptable for the individual member;
12. Member has not received prior gene therapy;
13. Provider attestation that alcohol abstinence education has been completed with the member;
14. Provider confirms that member will discontinue any use of hemophilia A prophylactic therapy within 4 weeks after administration of Roctavian;
15. Provider agrees to monitor the member according to the FDA-approved label (i.e., FVIII level tests, ALT monitoring and steroid treatment as appropriate);
16. Provider agrees to submit ALL of the following medical information after Roctavian administration upon plan request (a, b, and c):
    a. FVIII levels measured by the average of two consecutive chromogenic substrate assay or one stage assay measurements separated by one week;
    b. Documentation of all spontaneous bleeds after Roctavian administration (see Appendix D);
    c. Documentation of any resumed continuous hemophilia A prophylaxis and duration of prophylaxis;
17. Documentation of member's body weight in kg;
18. Dose does not exceed a single IV infusion of 6×10^{13} vector genomes (vg) per kg.

Approval duration: 3 months (*1 dose only*)

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Congenital Hemophilia A (must meet all)**:**

1. Continued therapy will not be authorized as Roctavian is indicated to be dosed one time only.

Approval duration: Not applicable

III. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

IV. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

V. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AAV: adeno-associated virus
ALP: alkaline phosphatase
ALT: alanine aminotransferase
AST: aspartate aminotransferase
BU: Bethesda unit
ED: exposure day
FDA: Food and Drug Administration
FVIII: factor VIII
GGT: gamma-glutamyl transferase
INR: international normalized ratio
LFT: liver function test
ULN: upper limit of normal
vg: vector genome
WFH: World Federation of Hemophilia

Appendix B: Therapeutic Alternatives

Drug Name	Usual Dosing Regimen	Dose Limit/ Maximum Dose
FVIII recombinant products for routine prophylaxis		
Advate®	20-40 IU/kg IV every other day (3 to 4 times weekly) or every third day dosing regimen targeted to maintain FVIII trough levels ≥ 1%	40 IU/kg every other day
Adynovate®	40-55 IU/kg IV 2 times per week	70 IU/kg/dose
Afstyla®	20-50 IU/kg IV 2-3 times per week	50 IU/kg/dose
Altuviiio®	50 IU/kg IV once weekly	50 IU/kg/dose
Eloctate®	50 IU/kg IV every 4 days	65 IU/kg/dose
Esperoct®	65 IU/kg IV twice weekly	65 IU/kg
Helixate FS®, Kogenate FS®	25 IU/kg IV three times per week	25 IU/kg/dose
Jivi®	45-60 IU/kg every 5 days with further individual adjustment to less or more frequent dosing	60 IU/kg/dose
Kovaltry®	20-40 IU/kg IV 2-3 times per week	50 IU/kg/dose
NovoEight®	20-50 IU/kg IV 3 times per week	60 IU/kg/dose
Nuwiq®	30-40 IU/kg IV every other day	50 IU/kg/dose
Xyntha®	30 IU/kg IV 3 times weekly	30 IU/kg/dose
Plasma-derived FVIII/von Willebrand factor complex for routine prophylaxis		
Wilate®	20-40 IU/kg IV every 2 to 3 days	40 IU/kg/day

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): active infections, either acute or uncontrolled chronic; known significant hepatic fibrosis (stage 3 or 4), or cirrhosis; known hypersensitivity to mannitol
- Boxed warning(s): none

Appendix D: General Information

- Serious bleeding episodes include bleeds in the following sites: intracranial; neck/throat; gastrointestinal; joints (hemarthrosis); muscles (especially deep compartments such as the iliopsoas, calf, forearm); or mucous membranes of the mouth, nose and genitourinary tract.
- Spontaneous bleed is defined as a bleeding episode that occurs without apparent cause and is not the result of trauma.
- An ED is a day on which a person with hemophilia has been infused with factor concentrate to treat or prevent a bleed. The number of EDs consists only of those days on which factor was infused.
    - 150 EDs of cumulative treatment increases the likelihood of immunologic stability – a decreased risk of producing inhibitors. Patients rarely develop inhibitors after 150 EDs.

VI. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Hemophilia A	Recommended dose: 6 x 10^{13} vg/kg body weight as a single IV infusion	6 x 10^{13} vg/kg body weight

VII. Product Availability

Single-dose cell suspension: nominal concentration of 2×10^{13} vg/mL with each vial containing an extractable volume of ≥ 8 mL

VIII. References

1. Roctavian Prescribing Information. Novato, CA: BioMarin Pharmaceutical; June 2023. Available at: https://investors.biomarin.com/download/ROCTAVIAN-Prescribing-Information_US.pdf. Accessed October 12, 2023.
2. Ozelo MC, Mahlangu J, Pasi KJ, et al. Valoctocogene roxaparvovec gene therapy for hemophilia A. N Engl J Med. 2022;386(11):1013-25.
3. Srivastava A, Santagostino E, Dougall A, et al. WFH Guidelines for the Management of Hemophilia, 3rd edition. Haemophilia. 2020;26 Suppl 6:1-158.
4. Medical and Scientific Advisory Council (MASAC) of the National Bleeding Disorders Foundation (formerly National Hemophilia Foundation): Database of treatment guidelines. Available at: https://www.hemophilia.org/healthcare-professionals/guidelines-on-care/masac-documents. Accessed October 26, 2023.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals
J3590	Unclassified drugs or biologicals

Reviews, Revisions, and Approvals	Date
Policy created	07/2023
1Q 2024 annual review: added exclusion for prior gene therapy per pivotal trial exclusion criteria; references reviewed and updated.	01/2024