Clinical Policy: Valoctocogene Roxaparvovec-rvox (Roctavian)

Reference Number: CP.PHAR.466
Effective Date: 06.29.23
Last Review Date: 02.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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.

All requests reviewed under this policy **require Precision Drug Action Committee (PDAC) Utilization Management Review**. Refer to CC.PHAR.21 for process details.

It is the policy of health plans affiliated with Centene Corporation® that Roctavian is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

**Only for initial treatment dose; subsequent doses will not be covered.*

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 meets both of the following (a and b):
   a. Member has been adherent with use of a FVIII product* for routine prophylaxis for at least 12 months as assessed and documented by provider;
   b. Occurrence of at least one serious spontaneous bleeding event while on routine prophylaxis *(see Appendix D)*;

   **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 (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
    a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Congenital Hemophilia A

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

Approval duration: Not applicable

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. 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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. 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.

V. 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

VI. Product Availability

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

VII. References

1. Roctavian Prescribing Information. Novato, CA: BioMarin Pharmaceutical; June 2023. Available at: https://www.roctavian.com/en-us/wp-content/uploads/sites/5/2023/07/ROC-ROCTAVIAN-Prescribing-Information-PI-DIGITAL.pdf?v=0.24. Accessed November 18, 2024.
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 November 18, 2024.
5. Rezende SM, Neumann I, Angchaisuksiri P, et al. International Society on Thrombosis and Haemostasis clinical practice guideline for treatment of congenital hemophilia A and B based on the Grading of Recommendations Assessment, Development, and Evaluation methodology. J Thromb Haemost. 2024;22(9):2629-2652.

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
J1412	Injection, valoctocogene roxaparvovec-rvox, per ml, containing nominal 2 x 10^{13} vector genomes

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2021 annual review: no significant changes as drug is not FDA-approved; references reviewed and updated; references to HIM.PHAR.21 revised to HIM.PA.154.	12.01.20	02.21
1Q 2022 annual review: no significant changes as drug is not yet FDA-approved; references reviewed and updated.	11.08.21	02.22
Removed "life-threatening" from "life-threatening or serious bleed" criterion as definition of what is serious vs life-threatening may not be mutually exclusive and there exists potential for misinterpretation.	05.09.22	
Template changes applied to other diagnoses/indications.	09.28.22	
1Q 2023 annual review: no significant changes as drug is not yet FDA-approved; references reviewed and updated.	10.20.22	11.22
Drug is now FDA-approved – criteria updated per FDA labeling: added criteria for baseline liver assessments and hepatologist attestation of Roctavian eligibility for abnormal results per PI; added criterion for provider attestation of member's ability to receive corticosteroids and/or other immunosuppressive therapy per PI; revised FVIII inhibitor level assay to be < 0.6 BU per clinical study protocols; added FVIII recombinant products indicated for routine prophylaxis in Appendix B; added criterion for member's weight in kg for dose calculation; added option for one stage assay measurement after Roctavian administration; updated sites of serious bleeds per WFH guideline in Appendix D; references reviewed and updated.	06.29.23	08.23
Added HCPCS code [J1412]	10.27.23	
1Q 2024 annual review: added exclusion for prior gene therapy per competitor analysis and pivotal trial exclusion criteria; references reviewed and updated.	10.27.23	02.24
1Q 2025 annual review: no significant changes; references reviewed and updated.	11.18.24	02.25
Added clarification statement to Policy/Criteria header that all requests reviewed under this policy require medical director review.	03.11.25	
Updated language under Policy/Criteria to effectively redirect prior authorization reviews to Precision Drug Action Committee (PDAC) Utilization Management Review.	11.04.25	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and

accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.