DR.015.A ROCTAVIAN™ (valoctocogene roxaparvovec-rvox)

Original Implementation Date : 05/15/2024
Version Version [A] Date : 05/15/2024
Last Reviewed Date: 05/21/2025

PRODUCT VARIATIONS

This policy applies to all Jefferson Health Plans/Health Partners Plans lines of business unless noted below.

Gene therapy is a benefit exclusion for Individual and Family (ACA) product lines and therefore, non-covered.

POLICY STATEMENT

The plan considers ROCTAVIAN™ (valoctocogene roxaparvovec-rvox) medically necessary for the treatment of adults with severe hemophilia A (congenital factor VIII deficiency with factor VIII activity < 1 IU/dL) without pre-existing antibodies to adeno-associated virus serotype 5 detected by an FDA-approved test when the prior authorization criteria listed in the policy are met. The plan considers the use of ROCTAVIAN™ experimental and investigational for all other indications.

FDA APPROVED INDICATIONS

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 pre-existing antibodies to adeno-associated virus serotype 5.

OFF-LABEL USE

N/A

PRIOR AUTHORIZATION CRITERIA

INITIAL CRITERIA

*AUTHORIZATION DURATION: IF **ALL CRITERIA MET**, APPROVE FOR 1 DOSE FOR 1 MONTH*

1. The patient is 18 years of age or older.
2. The patient was assigned male at birth.
3. Prescriber is or in consultation with a hematologist or a prescriber who specializes in hemophilia A.
4. The dose prescribed is consistent with U.S. Food and Drug Administration (FDA) approved package labeling, nationally recognized compendia, or peer-reviewed medical literature.
5. Patient has a diagnosis of severe hemophilia A as defined by a factor VIII levels less than 1% of normal factor VIII (< 0.01 IU/mL, < 1 IU/dL).
6. Patient has an FDA-approved test showing NO detectable pre-existing antibodies to adenoassociated virus 5 (AAV5).
7. Patient does not have prior or active factor VIII inhibitors (inhibitor titer must be less than 0.6 Bethesda Units {BU} using the Nijmegen-Bethesda assay).
8. Patient has received an ultrasound and elastography or laboratory assessments for liver fibrosis.
9. Patient has a history of Factor VIII therapy for at least 150 exposure days.
10. Patient has not received treatment with the requested medication previously.
11. Patient does not have a known hypersensitivity to mannitol.
12. Patient has documentation of a negative hepatitis B and/or hepatitis C infection.
13. Patient does not have a history of thrombosis or thrombophilia.
14. Provider attestation that member has been counseled regarding the risks of alcohol consumption and use of concomitant hepatotoxic medications after receiving Roctavian™ and member agrees to abstain from alcohol consumption for at least 1 year following infusion.
15. Provider attestation that member has been counseled that for a period of up to 6 months after administration of Roctavian™ a male of reproductive potential (and his female partner) should prevent or postpone pregnancy by utilizing an effective form of contraception; a male should not donate semen.

16. Provider attestation that after the gene therapy regular prophylactic therapy will be discontinued following an appropriate time for FVIII to reach therapeutic levels. (Use of episodic Factor VIII therapy is acceptable for the treatment of bleeds and for surgery/procedures if needed as determined by the hemophilia specialist physician).

RENEWAL CRITERIA

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The plan considers continued use of ROCTAVIAN™ experimental and investigational as the safety and efficacy beyond one dose has not been studied. Approval is limited to one treatment course per lifetime.

DOSAGE AND ADMINISTRATION

Clear, colorless to pale yellow suspension for intravenous infusion containing 2×10^{13} vg valoctocogene roxaparvovec-rvox per mL. Provided in vials containing an extractable volume of not less than 8 mL. Dose volume is based on body weight, with a recommended dose of 6×10^{13} vg/kg.

Dosing Recommendations:

- The recommended dose of is 6×10^{13} vector genomes per kilogram (vg/kg) body weight, administered as a single intravenous infusion. Administer with a single infusion pump at a rate of 1 mL/min, which can be increased every 30 seconds by 1 mL/min up to a maximum rate of 4 mL/min.

- Calculating Dose in Milliliters (mL) and Number of Vials Required:
    - Patient dose volume in mL:
        - Body weight in kilograms (kg) multiplied by 3 = dose in mL.
        - The multiplication factor 3 represents the per kilogram dose (6×10^{13} vg/kg) divided by the amount of vector genomes per mL of the suspension (2×10^{13} vg/mL).
    - Number of vials to be thawed:
        - Patient dose volume (mL) divided by 8 = number of vials to be thawed (round up to the next whole number of vials).
        - The division of 8 represents the minimum volume extractable from a vial (8 mL).
- Administered only once.

Administration:

- Administer in a setting where personnel and equipment are immediately available to treat infusion-related reactions.
- Infuse the suspension through a suitable peripheral vein, using an infusion catheter.
- For one-time single-dose intravenous use only.
- Treatment should be supervised by a physician experienced in hemophilia and/or bleeding disorders.

For Patient Selection

- Perform testing for pre-existing antibodies to AAV5 using the FDA approved companion diagnostic. **DO NOT** administer to patients with a positive test for antibodies to AAV5.
- Perform factor VIII inhibitor titer testing.
- **DO NOT** administer to a patient with a positive test for factor VIII inhibitor.
- Perform liver health assessments, which include:
    - Liver function tests [alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP), total bilirubin and international normalized ration (INR)].
    - Ultrasound and elastography or laboratory assessments for liver fibrosis in case of radiological liver abnormalities and/or liver function test abnormalities (ALT, AST, GGT, ALP or total bilirubin > 1.25 × ULN or INR ≥ 1.4), consider a consultation with a hepatologist to assess eligibility for Roctavian.
    - Assess patient's ability to receive corticosteroids and/or other immunosuppressive therapy that may be required for an extended period. Ensure that the risks associated with immunosuppression are acceptable for the individual patient.
- **DO NOT** administer to patients with active acute or uncontrolled chronic infections, known significant hepatic fibrosis (stage 3 or 4 on the Batts-Ludwig scale or equivalent) or cirrhosis, or mannitol hypersensitivity.

RISK FACTORS/SIDE EFFECTS

- *Infusion-related reactions:* Infusion reactions, including hypersensitivity reactions and anaphylaxis, have occurred. Monitor during and for at least 3 hours after administration. If symptoms occur, slow or interrupt administration and give appropriate treatment. Restart infusion at slower rate once symptoms resolve. Discontinue infusion for anaphylaxis.
- *Hepatotoxicity:* Monitor alanine aminotransferase (ALT) weekly for at least 26 weeks and institute corticosteroid treatment in response to ALT elevations as required. Continue to

monitor ALT until it returns to baseline. Monitor factor VIII activity levels since ALT elevation may be accompanied by a decrease in factor VIII activity. Monitor for and manage adverse reactions from corticosteroid use.

- *Thromboembolic events:* Thromboembolic events may occur in the setting of elevated factor VIII activity above the upper limit of normal (ULN). Factor VIII activity above ULN has been reported following infusion. Evaluate for risk factors for thrombosis including cardiovascular risk factors prior to and after use and advise patients accordingly.

- *Malignancy:* Monitor for hepatocellular malignancy in patients with risk factors for hepatocellular carcinoma (e.g., hepatitis B or C, non-alcoholic fatty liver disease, chronic alcohol consumption, non-alcoholic steatohepatitis, advanced age). Perform regular liver ultrasound (e.g., annually) and alpha-fetoprotein testing following administration.

- *Monitoring laboratory tests:* Monitor for factor VIII activity and factor VIII inhibitors.

- *Most common adverse reactions* (incidence ≥ 5%) were nausea, fatigue, headache, infusion-related reactions, vomiting, and abdominal pain.

- *Most common laboratory abnormalities* (incidence ≥ 10%) were ALT, aspartate aminotransferase (AST), lactate dehydrogenase (LDH), creatine phosphokinase (CPK), factor VIII activity levels, gamma-glutamyl transferase (GGT) and bilirubin > ULN.

MONITORING

Factor VIII Assays

- Factor VIII activity produced by in human plasma is higher if measured with OSA compared to CSA. In clinical studies, there was a high correlation between OSA and CSA factor VIII activity levels across the entire range of each assay's results. For routine clinical monitoring of factor VIII activity levels, either assay may be used. The conversion factor between the assays can be approximated based on clinical study results (central laboratory) to be: OSA = 1.5 × CSA. For example, a factor VIII activity level of 50 IU/dL using CSA calculates to a level of 75 IU/dL using OSA. The OSA to CSA ratio depends on the factor VIII assay reagents used by the laboratory and can range from 1.3 to 2.0, therefore, the same type of OSA or CSA reagents should be used to monitor factor VIII levels over time.

- When switching from hemostatic products prior to treatment, physicians should refer to the relevant prescribing information to avoid the potential for factor VIII activity assay interference during the transition period.

Factor VIII Inhibitors

- Monitor patients through appropriate clinical observations and laboratory tests for the development of factor VIII inhibitors after administration. Perform an assay that detects factor VIII inhibitors if bleeding is not controlled, or plasma factor VIII activity levels decrease.

BLACK BOX WARNING

N/A

BACKGROUND

Hemophilia A is an X-linked recessive bleeding disorder caused by a deficiency of coagulation factor VIII (hemophilia A), factor IX (hemophilia B), or factor XI (hemophilia C). It is estimated about 400 babies per year are born with hemophilia A and affects 1 in 5,000 male births. Most are inherited cases, diagnosed at a young age, although some rare cases are developed later in life.

Clinical Manifestations Patients with hemophilia A who produce less than 1% of normal levels of factor VIII have the most severe form of the condition, accounting for roughly half of all hemophilia A patients (FDA 2022). Hemarthrosis, a hallmark of severe hemophilia, is a major cause of disability. Recurrent bleeds lead to joint contractures, and pseudotumors, resulting in chronic pain, disability, and a diminished quality of life.

Current standard of care: (Clotting Factor Replacement Therapy) remains the main treatment for severe Hemophilia A. These treatments are used during bleeding episodes or prophylactically to prevent bleeds.

Treatment History: Developed by BioMarin Pharmaceutical for hemophilia A, received orphan drug status from the FDA in 2016 and breakthrough therapy designation in 2017. It faced initial FDA rejection due to durability concerns but was approved in the EU in August 2022 and in the US in June 2023, targeting adults with severe hemophilia A lacking antibodies to AAV5 virus.

CODING

Note*:* The Current Procedural Terminology (CPT®), Healthcare Common Procedure Coding System (HCPCS), and the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes that *may* be listed in this policy are for reference purposes only. Listing of a code in this policy does not imply that the service is covered and is not a guarantee of payment. Other policies and coverage guidelines may apply. When reporting services,

providers/facilities should code to the highest level of specificity using the code that was in effect on the date the service was rendered. This list may not be all inclusive.

CPT® is a registered trademark of the American Medical Association.

CPT Code	Description
N/A	N/A

HCPCS Code	Description
J1412	Injection, valoctocogene roxaparvovec-rvox

ICD-10 Codes	Description
D66	• Classic Hemophilia • Deficiency Factor VIII • Hemophilia A • Hemophilia NOS • Hereditary Factor VIII deficiency

DISCLAIMER

Approval or denial of payment does not constitute medical advice and is neither intended to guide nor influence medical decision making. Policy Bulletins are developed to assist in administering plan benefits and constitute neither offers of coverage nor medical advice. This Policy Bulletin may be updated and therefore is subject to change. For Health Partners Plans Medicaid and Health Partners Plans Chip products: Any requests for services that do not meet criteria set in PARP will be evaluated on a case-by-case basis.

POLICY HISTORY

This section provides a high-level summary of changes to the policy since the previous version.

Summary	Version	Version Date

2025 Annual Review. References updated.	A	05/15/2024
New Policy.	A	05/15/2024

REFERENCES

1. Centers for Disease Control and Prevention. Treatment of Hemophilia. 20243 Nov 13. Available from:https://www.cdc.gov/hemophilia/treatment/?CDC_AAref_Val=https://www.cdc.gov/ncbddd/hemophilia/treatment.html. Accessed March 14, 2024.

2. Roctavian™ [package insert]. Novato, CA; BioMarin Pharmaceutical, Inc: June 2023

3. BioMarin. Is Roctavian™ Right for You? Roctavian™. Available from: https://www.roctavian.com/en-us/is-roctavian-right-for-you. Accessed March 14, 2024.

4. Centers of Disease Control and Prevention. Data & Statistics on Hemophilia. 2024 May15. Available from: https://www.cdc.gov/hemophilia/data-research/?CDC_AAref_Val=https://www.cdc.gov/ncbddd/hemophilia/data.htmlAccessed March 14, 2024.

5. National Library of Medicine. A Study to Evaluate the Efficacy and Safety of Valoctocogene Roxaparvovec, in Hemophilia A Patients (GenEr8-1). NCT02576795. https://clinicaltrials.gov/ct2/show/NCT02576795. Accessed March 14, 2024.