Medical Policy:
Roctavian (valoctocogene roxaparvovec)

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.397	January 9, 2024	October 13, 2023

Definitions

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. Valoctocogene roxaparvovec-rvox is an adeno-associated virus serotype 5 (AAV5) based gene therapy vector, designed to introduce a functional copy of a transgene encoding the B-domain deleted SQ form of human coagulation factor VIII (hFVIII-SQ). Transcription of this transgene occurs within the liver, using a liver-specific promoter, which results in the expression of hFVIII-SQ. The expressed hFVIII-SQ replaces the missing coagulation factor VIII needed for effective hemostasis.

Length of Authorization

1 course per lifetime

Dosing Limits [Medical Benefit]

The recommended dose is 6×10^{13} vector genomes (vg) per kg of body weight (44 vials one time only)

Guideline

I. INITIAL CRITERIA

1. **Hemophilia A**

A. The patient has a diagnosis of hemophilia A (also known as Factor VIII deficiency, or classic hemophilia) **AND**

B. The patient's sex is male **AND**

C. The patient is 18 years of age or over **AND**

D. The patient has severe hemophilia A as evidence by a Factor VIII baseline (without Factor VIII replacement therapy) residual level less than or equal to 1 IU/dL (lab test required) **AND**

E. The patient does not have anti-AAV antibodies (e.g., AAV-5) titers that exceed labeling administration instructions (test results within the past 3 months required) **AND**

F. The patient is on prophylactic therapy with a Factor VIII agent (e.g., Advate, Eloctate, Recombinate) **AND** has had a minimum of 150 exposure days; **AND**

G. The Patient meets all of the following (i, ii, and iii):

i. Factor VIII inhibitor titer testing has been performed within 30 days before intended receipt of Roctavian; **AND**

ii. The patient does NOT have active inhibitors to Factor VIII **AND**

iii. Patient does not have a history of Factor VIII inhibitors; **AND**

H. Prophylactic therapy with Factor VIII will not be given after Roctavian administration once adequate Factor VIII levels have been achieved; **AND**

Note: 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.

I. The patient has **NOT** had previous gene therapy for hemophilia A (including requested agent); **AND**

J. Patient does not have a known hypersensitivity to mannitol; **AND**

K. The patient does **NOT** have another active acute or uncontrolled chronic infection **AND**

L. The Patient does not have chronic or active hepatitis B **AND**

M. Patient does not have active hepatitis C **AND**

N. Patient does not have evidence of significant hepatic fibrosis or cirrhosis; **AND**

O. Patient meets one of the following (i or ii):

i. Patient has undergone a liver health assessment within 30 days before intended receipt of Roctavian and meets all of the following (a, b, c, d, e, and f):

a. Alanine aminotransferase levels are ≤ 1.25 times the upper limit of normal; **AND**

b. Aspartate aminotransferase levels are ≤ 1.25 times the upper limit of normal; **AND**

c. Total bilirubin levels are ≤ 1.25 times the upper limit of normal; **AND**

d. Alkaline phosphatase levels are ≤ 1.25 times the upper limit of normal; **AND**

e. Gamma-glutamyl transferase levels are ≤ 1.25 times the upper limit of normal; **AND**

f. The International Normalized Ratio is < 1.4; **OR**

ii. If the patient had one or more of the laboratory values listed in *Criteria a-f* above that was not at the value specified in *Criteria a-f* above, then a hepatologist has evaluated the patient and has determined that use of Roctavian is clinically appropriate; **AND**

P. Within 30 days before intended receipt of Roctavian, the platelet count was ≥ 100 x 10^9/L; **AND**

Q. Within 30 days before intended receipt of Roctavian, the creatinine level was < 1.4 mg/dL **AND**

R. Patient has not used a systemic immunosuppressive agent within 30 days before intended receipt of Roctavian; **AND**

Note: Corticosteroids are not included as systemic immunosuppressive agents.

S. Patient does not have any disease or condition that would interfere with the compliance requirements that involve use of systemic corticosteroid therapy or systemic alternative immunosuppressive medications; **AND**

T. Patient does not have an immunosuppressive disorder; **AND**

U. The patient is NOT HIV positive (medical records including lab tests within the past 3 months required); **AND**

V. The patient does **NOT** have evidence of any bleeding disorder not related to hemophilia A **AND**
W. Patient does not have a history of thrombosis or thrombophilia; **AND**
X. Patient does not have a current active malignancy; **AND**
Note: Current active malignancy does not include non-melanoma skin cancer.
Y. Patient does not have a history of hepatic malignancy; **AND**
Z. Patient has not received a live vaccine within 30 days before intended receipt of Roctavian; **AND**
AA. The hemophilia specialist physician has discussed with the patient that for a period of up to 6 months after administration of Roctavian the following precautions should be taken (i and ii):
    i. A male of reproductive potential (and his female partner) should prevent or postpone pregnancy by utilizing an effective form of contraception; **AND**
    ii. A male should not donate semen; **AND**
BB. Medication is prescribed by a hemophilia specialist physician**; AND**
CC. Current patient body weight has been obtained within 30 days before intended receipt of Roctavian

Applicable Procedure Codes

Code	Description
J1412	Roctavian Suspension, Injection, valoctocogene roxaparvovec-rvox, per ml, containing nominal 2 x 10^13 vector genomes

Applicable NDCs

Code	Description
68135-0927-01	Roctavian Suspension
68135-0927-48	Roctavian Suspension

ICD-10 Diagnoses

Code	Description
D66	Hereditary factor VIII deficiency

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	1/9/2024	Annual Review: removed J3590. C9399, added J1412 Initial Criteria: Hemophilia A Removed: "The prescriber has provided information that the requested agent is medically appropriate for the patient's sex (medical records required) AND" Added: "The patient has severe hemophilia A as evidence by" to the statement a Factor VIII baseline (without Factor VIII replacement therapy) residual level less than or equal to 1 IU/dL (lab test required) Removed: "The patient has a Factor VIII baseline residual level greater than 1 IU/dL and less than or equal to 5 IU/dL AND the prescriber has determined that the patient has a bleed history that simulates severe hemophilia A (medical records including lab test and bleed history required) AND The prescriber has determined that the patient requires improved protection than they are receiving from their current therapy (e.g., patients with increased bleeding due to severely damaged joints, patients with

		increased bleeding due to need for anticoagulation, elderly patients with risk for falls) AND" Added: "Factor VIII inhibitor titer testing has been performed within 30 days before intended receipt of Roctavian; AND Patient does not have a history of Factor VIII inhibitors; AND Prophylactic therapy with Factor VIII will not be given after Roctavian administration once adequate Factor VIII levels have been achieved; AND Patient does not have a known hypersensitivity to mannitol; AND" Reworded for clarity: "The patient does NOT have another active acute or uncontrolled chronic infection AND" Reworded "The patient's hepatitis B surface antigen is negative (medical records including lab tests within the past 3 months required) Patient does not have chronic or active hepatitis B AND The patient has ONE of the following: The patient's hepatitis C virus (HCV) antibody is negative (medical records including lab tests within the past 3 months required) OR The patient's HCV antibody is positive AND the patient's HCV RNA is negative (medical records including lab tests within the past 3 months required)" to " Patient does not have active hepatitis C AND" Reworded "Patient does not have evidence of significant hepatic fibrosis or cirrhosis; AND Patient meets one of the following (i or ii): Patient has undergone a liver health assessment within 30 days before intended receipt of Roctavian and meets all of the following (a, b, c, d, e, and f): Alanine aminotransferase levels are ≤ 1.25 times the upper limit of normal; AND Aspartate aminotransferase levels are ≤ 1.25 times the upper limit of normal; AND Total bilirubin levels are ≤ 1.25 times the upper limit of normal; AND Alkaline phosphatase levels are ≤ 1.25 times the upper limit of normal; AND Gamma-glutamyl transferase levels are ≤ 1.25 times the upper limit of normal; AND The International Normalized Ratio is < 1.4; OR If the patient had one or more of the laboratory values listed in Criteria a-f above that was not at the value specified in Criteria a-f above, then a hepatologist has evaluated the patient and has determined that use of Roctavian is clinically appropriate [documentation required]; AND" From this prior statement: "The patient does NOT have significant liver dysfunction as defined by abnormal elevation of any of the following: (lab results within the past 3 months required) ALT (alanine transaminase) 3 times the upper limit of normal Bilirubin above 3 times the upper limit of normal Alkaline phosphatase above 3 times the upper limit of normal INR (international normalized ratio) greater than or equal to 1.4 AND" Added: "Within 30 days before intended receipt of Roctavian, the platelet count was ≥ 100 x 10^9/L; AND" Reworded: "The patient does NOT have creatinine greater than or equal to 1.5 mg/dL (lab results within the past 3 months required)" to "Within 30 days before intended receipt of Roctavian, the creatinine level was < 1.4 mg/dL AND" Added: "Patient has not used a systemic immunosuppressive agent within 30 days before intended receipt of Roctavian; AND. Patient does not have any disease or condition that would interfere with the compliance requirements that involve use of systemic corticosteroid therapy or systemic alternative immunosuppressive medications; AND" Reworded to remove the following"The patient is HIV positive AND is well controlled (i.e. viral load within the past 12 months less than 1000 copies/mL) (lab results within the past 12 months required)" Added: "Patient does not have a history of thrombosis or thrombophilia; AND Patient does not have a current active malignancy; AND Patient does not have a history of hepatic malignancy; AND Patient has not received a live vaccine within 30 days before intended receipt of Roctavian; AND The hemophilia specialist physician has discussed with the patient that for a period of up to 6 months after administration of Roctavian the following precautions should be taken (i and ii):

		A male of reproductive potential (and his female partner) should prevent or postpone pregnancy by utilizing an effective form of contraception; AND A male should not donate semen; AND Medication is prescribed by a hemophilia specialist physician; AND Current patient body weight has been obtained within 30 days before intended receipt of Roctavian" Removed: "The patient has a modified Nijmegen Bethesda assay of less than 0.6 Bethesda Units (BU) on 2 consecutive occasions at least one week apart within the past 12 months (test results required) AND The patient is NOT on any bypassing agents (i.e., Feiba, NovoSeven) AND"
EmblemHealth & ConnectiCare	10/13/2023	New Policy

References

1. Roctavian (valoctocogene roxaparvovec) [prescribing information]. Novato, CA: BioMarin Pharmaceuticals Inc; June 2023.