Drug and Biologic Coverage Policy

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Coverage Policy Number IP0580

Valoctocogene roxaparvovec-rvox

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for valoctocogene roxaparvovec-rvox (Roctavian®).

Gene Therapy coverage varies across plans. Refer to the customer's benefit plan document for coverage details.

Medical Necessity Criteria

Valoctocogene roxaparvovec-rvox (Roctavian) is considered medically necessary when the following are met:

1. **Hemophilia A.** Individual meets **ALL** of the following criteria:
   A. Male
   B. 18 years of age or older
   C. Documentation of severe hemophilia A as evidenced by a baseline (without Factor VIII replacement therapy) Factor VIII level of less than 1 IU/dL

D. Documentation by an FDA-approved test showing no detectable pre-existing antibodies to adeno-associated virus 5 (AAV5)
E. Has a history of use of Factor VIII therapy for at least 150 exposure days
F. Documentation of **ALL** of the following:
    i. Factor VIII inhibitor titer testing has been performed within 30 days before intended receipt of Roctavian
    ii. Does not currently have an inhibitor to Factor VIII
    iii. Does not have a history of Factor VIII inhibitors
G. Prophylactic therapy with Factor VIII will not be given once adequate Factor VIII levels have been achieved

    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.

H. Has not received Roctavian in the past
I. Does not have a known hypersensitivity to mannitol
J. Does not have an active acute or uncontrolled chronic infection
K. Does not have chronic or active hepatitis B
L. Does not have active hepatitis C
M. Does not have evidence of significant hepatic fibrosis or cirrhosis
N. Documentation of **ONE** of the following:
    i. Has undergone a liver health assessment within 30 days before intended receipt of Roctavian and meets **ALL** of the following:
        a. Alanine aminotransferase levels are less than or equal to 1.25 times the upper limit of normal
        b. Aspartate aminotransferase levels are less than or equal 1.25 times the upper limit of normal
        c. Total bilirubin levels are less than or equal 1.25 times the upper limit of normal
        d. Alkaline phosphatase levels are less than or equal 1.25 times the upper limit of normal
        e. Gamma-glutamyl transferase levels are less than or equal 1.25 times the upper limit of normal
        f. The International Normalized Ratio is less than 1.4
    ii. If had one or more of the laboratory values listed in criteria above (a-f) that was not at the value specified, then a hepatologist has evaluated the individual and has determined that use of Roctavian is clinically appropriate
O. Documentation that within 30 days before intended receipt of Roctavian, the platelet count was at least 100 x 10^9/L
P. Documentation that within 30 days before intended receipt of Roctavian, the creatinine level was less than 1.4 mg/dL
Q. Has not used a systemic immunosuppressive agent within 30 days before intended receipt of Roctavian

    Corticosteroids are not included as systemic immunosuppressive agents.

R. 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
S. Does not have an immunosuppressive disorder
T. Documentation showing negative for human immunodeficiency virus
U. Does not have any additional bleeding disorder, besides hemophilia A
V. Does not have a history of thrombosis or thrombophilia
W. Does not have a current active malignancy

    Current active malignancy does not include non-melanoma skin cancer.

X. Does not have a history of hepatic malignancy
Y. Has not received a live vaccine within 30 days before intended receipt of Roctavian
Z. Hemophilia specialist physician has discussed with the indiviudal that for a period of up to 6 months after administration of Roctavian the following precautions should be taken:
   i. A male of reproductive potential (and his female partner) should prevent or postpone pregnancy by utilizing an effective form of contraception
   ii. A male should not donate semen
AA. Medication is prescribed by a hemophilia specialist physician
BB. Documented current body weight obtained within 30 days before intended receipt of Roctavian
CC. If criteria A through BB are met, one dose of Roctavian will be approved to provide a one-time (per lifetime) dose of 6 x 10^{13} vector genomes per kg by intravenous infusion

Roctavian is supplied in a carton (NDC 68135-0927-48) that contains one single dose vial (NDC 68135-927-01) with an extractable volume of not less than 8 mL, containing 16 x 10^{13} vector genomes.

Dosing. The recommended dose of Roctavian is a single one-time (per lifetime) intravenous infusion of 6 x 10^{13} vector genomes per kilogram based on current body weight in kilograms.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Authorization Duration

Authorization is for a single one-time approval.

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J3490	Unclassified drug
J3590	Unclassified biological

Background

OVERVIEW
Roctavian, an adeno-associated virus vector-based gene therapy, is 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 detected by an FDA-approved test.[1]

Disease Overview
Hemophilia A is an X-linked bleeding disorder primarily impacting males caused by a deficiency in Factor VIII.[2-7] In the US, the incidence of hemophilia A in males is 1:5,000 with an estimated 20,000 people in the US living

with hemophilia A. The condition is characterized by bleeding in joints, either spontaneously or in a provoked joint. Bleeding can occur in many different body areas as well (e.g., muscles, central nervous system). The bleeding manifestations can lead to substantial morbidity such as hemophilic arthropathy. Disease severity is usually defined by the plasma levels or activity of Factor VIII classified as follows: severe (< 1 IU/dL), moderate (1 IU/dL to 5 IU/dL), and mild (> 5 IU/dL to < 40 IU/dL); phenotypic expression may vary. Approximately 50% of patients with hemophilia A are categorized as having severe disease. These patients usually require routine prophylaxis with Factor VIII replacement therapy products or Hemlibra® (emicizumab subcutaneous injection) to prevent bleeding.

Clinical Efficacy

The efficacy of Roctavian was evaluated in one open-label, single-group, multinational Phase III trial (GENEr8-1) involving 134 adult males (≥ 18 years of age) with severe hemophilia A (Factor VIII activity level ≤ 1 IU/dL).[1,8,9] Patients involved in the trial did not have Factor VIII inhibitors (or a history of such inhibitors) and were receiving regular prophylaxis with Factor VIII products. Use of prophylactic Factor VIII therapy was not permitted during the trial, but could be used up to 4 weeks post Roctavian administration to allow the agent to have an effect. Other notable exclusion criteria were active infection, chronic or active hepatitis B or C, immunosuppressive disorder (including HIV), Stage 3 or 4 liver fibrosis, cirrhosis, liver function test abnormalities, a history of thrombosis or thrombophilia, serum creatinine ≥ 1.4 mg/dL, and active malignancy. Patients had to be treated or exposed to Factor VIII concentrates previously for a minimum of 150 exposure days. Use of systemic immunosuppressive agents (not including corticosteroids), or live vaccines within 30 days before Roctavian infusion prevented participation. In the 132 patients who completed more than 51 weeks of follow-up (and were HIV-negative), the mean Factor VIII activity level at Weeks 49 through 52 had increased by 41.9 IU/dL (a non-hemophilic range). Among the 112 patients enrolled from a noninterventional study who had baseline annualized bleeding rate information prospectively collected for at least 6 months before receiving Roctavian (the rollover population), the mean annualized rates of Factor VIII concentrate use and treated bleeding after Week 4 had decreased after Roctavian administration by 98.6% and 83.8%, respectively ($P < 0.001$ for both comparisons). At Year 3 post Roctavian dosing the mean annualized bleeding rate in the rollover population in the efficacy evaluation period was 2.6 bleeds/year compared to a mean baseline of 5.4 bleeds/year (while using Factor VIII therapies); mean Factor VIII activity levels were 21 IU/dL at this timepoint (mild hemophilic range).

References

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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. *Lance*t. 2021;397:630-640.
5. Croteau SE. Hemophilia A/B. *Hematol Oncol Clin North Am*. 2022;36(4):797-812.
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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.
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9. Mahlangu J, Kaczmarek R, Von Drygalski A, et al, for the GENEr8-1 trial group. Two-year outcomes of valoctocogene roxaparvovec therapy for hemophilia A. *N Engl J Med*. 2023;388(8):694-705.

Revision History

Type of Revision	Summary of Changes	Approval Date
New		9/26/2023