# Roctavian (valoctocogene roxaparvovec-rvox)



## Summary

Hemophilia A is a rare, X-linked genetic bleeding disorder caused by coagulation factor VIII deficiency. Based on the level of clotting factor (factor VIII) activity detected in the blood, hemophilia A severity is classified into the following categories:

1. Severe disease - Factor VIII activity less than 1% of normal (less than 1 unit/dL)
2. Moderate disease - Factor VIII activity between 1% to 5% of normal (1 to 5 units/dL)
3. Mild disease - Factor VIII activity more than 5% but less than 49% of normal (more than 5 but less than 49 units/dL)

Patients with severe hemophilia A are at high risk for spontaneous bleeding episodes, particularly into joints and muscles, leading to chronic pain, joint damage, and disability. The current standard of care is routine intravenous prophylactic infusions of factor VIII concentrate to prevent bleeding events. However, breakthrough bleeding still occurs due to the short 8-12 hour half-life of factor VIII products.

Roctavian (valoctocogene roxaparvovec-rvox) is the first gene therapy approved for adults with severe hemophilia A. It delivers a functional F8 gene via an adeno-associated virus serotype 5 (AAV5) viral vector to enable endogenous factor VIII production. It 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 AAV5 detected by an FDA-approved test.

- It is administered as a one-time intravenous infusion.
- It provides an alternative to intravenous factor VIII prophylaxis, but is not a cure for hemophilia A.
- In the phase 3 trial, Roctavian (valoctocogene roxaparvovec-rvox) reduced annualized bleeding rates by 52% over 3 years. However, factor VIII activity wanes over time.

## Definitions

"AAV5 Viral Vector" is a tool used in gene therapy to deliver a functional F8 gene to cells. AAV5 is a specific type of adeno-associated virus.

"Annualized Bleeding Rates" refers to the expected number of bleeding episodes within a year.

"Antibodies to AAV5" are proteins produced by the immune system that recognize and neutralize the AAV5 virus, potentially impacting the efficacy of Roctavian.

"Bethesda Assay" is a laboratory test used to measure the level of factor VIII inhibitors in the blood.

"Factor VIII Inhibitors" are proteins produced by the immune system that neutralize factor VIII, making treatment less effective.

"Factor VIII" is a protein involved in blood clotting. Its deficiency leads to Hemophilia A.

"FDA" refers to the United States Food and Drug Administration, responsible for approving drugs and medical treatments.

"Hemophilia A" is a rare, X-linked genetic bleeding disorder resulting from a deficiency in coagulation factor VIII.

"Prophylactic Infusions" refers to preventive treatment given to avoid the onset of a disease or condition, in this case, bleeding episodes.

"Thrombocytopenia" is a condition characterized by low platelet count, leading to increased risk of bleeding.

"Vector Genomes" are complete sets of viral DNA. In this context, it's used to measure the dosage of Roctavian.

"Von Willebrand Disease" is a genetic disorder caused by missing or defective von Willebrand factor (VWF), a clotting protein.

"X-linked" refers to a gene carried on the X chromosome. In the context of hemophilia, it primarily affects males since they have only one X chromosome.

## Medical Necessity Criteria for Authorization

The Plan considers Roctavian (valoctocogene roxaparvovec-rvox) medically necessary when ALL of the following criteria are met:

1. Prescribed by or in consultation with a physician experienced in the treatment of hemophilia and/or bleeding disorders (e.g., hematologist); *AND*
    a. IF there is documentation indicating any radiological liver irregularities or liver function test anomalies (ALT, AST, GGT, ALP or total bilirubin > 1.25 times the upper limit of normal [ULN] or INR ≥ 1.4), a consultation with a hepatologist is required; *AND*
2. The member is 18 years of age or older; *AND*
3. The member has a diagnosis of severe hemophilia A, defined as congenital factor VIII deficiency with factor VIII activity level less than or equal to (≤) 1 IU/dL; *AND*
4. Documentation of ALL of the following :
    a. Baseline testing for BOTH of the following:
        i. Factor VIII inhibitor titer; *and*
        ii. Preexisting antibodies to adeno-associated virus serotype 5 (AAV5)[※]; *and*
    b. At least 6 months prophylactic use of factor VIII before considering Roctavian; *and*
    c. Liver health assessments, which include:
        i. Liver function tests, i.e., ALT, AST, GGT, ALP, total bilirubin, and INR; *and*
        ii. Liver condition evaluations through ultrasound, elastography, or laboratory assessments for liver fibrosis; *and*
    d. Documentation that the provider has educated on, and reviewed the member's prior medical and medication history for the risk of hepatotoxicity; *AND*

    [※]*Information on approved tests is available at fda.gov/CompanionDiagnostics.*
5. The member meets ALL of the following criteria:
    a. No evidence of active infections, either acute (such as acute respiratory infections or acute hepatitis) or uncontrolled chronic (such as chronic active hepatitis B); *and*
    b. No evidence of hypersensitivity to mannitol; *and*
    c. No evidence of the presence of antibodies to AAV5 capsid, as confirmed by an FDA-approved/cleared or CLIA-compliant test[※], such as ARUP Laboratories' AAV5 DetectCDx™; *and*
    d. No evidence of the presence of factor VIII inhibitors (i.e., results from a Bethesda assay or Bethesda assay with Nijmegen modification of less than 0.6 Bethesda Units (BU)); *and*
    e. No evidence of stage 3 or 4 liver fibrosis, or cirrhosis; *AND*

6. Authorization is for no more than:
    a. The recommended dose of $6 \times 10^{13}$ vector genomes per kilogram (vg/kg) body weight, administered as a single intravenous infusion; *or*
    b. One dose of Roctavian (valoctocogene roxaparvovec-rvox) per lifetime.

<u>If the above criteria are met, one dose of Roctavian (valoctocogene roxaparvovec-rvox) will be approved for the one-time treatment for 6 months.</u>

## Experimental or Investigational / Not Medically Necessary

Roctavian (valoctocogene roxaparvovec-rvox) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

1. Hemophilia A (congenital factor VIII deficiency) in the following cases:
    a. Retreatment after receiving one prior dose.
    b. Dosage exceeding the FDA-approved dose of $6 \times 10^{13}$ vector genomes per kilogram (vg/kg) body weight.
    c. Use in females. Roctavian (valoctocogene roxaparvovec-rvox) has only been studied in males.
    d. Use in those with pre-existing antibodies to adeno-associated virus serotype 5 (AAV5).
    e. Use in those with current or prior factor VIII inhibitors.
    f. Use in those less than 18 years of age. Roctavian (valoctocogene roxaparvovec-rvox) has not been studied in the pediatric population.
    g. Mild or moderate hemophilia A defined as:
        i. Mild: Factor VIII level 6% to 49%.
        ii. Moderate: Factor VIII level 1% to 5%.
2. Treatment of other coagulation factor deficiencies (e.g. factors IX, XI, XII). Roctavian (valoctocogene roxaparvovec-rvox) has only been studied in those with severe hemophilia A and a Factor VIII deficiency.
3. Treatment of thrombocytopenia or platelet dysfunction.
4. Treatment of vitamin K deficiency.
5. Treatment of von Willebrand disease.

## Applicable Billing Codes (HCPCS/CPT Codes)

| *Service(s) name* |
| --- |
| CPT/HCPCS Codes considered medically necessary if criteria are met: |

| *Code* | *Description* |
|---|---|
| 96365 | Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour |
| 96366 | Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure) |
| 99221 | Initial hospital inpatient or observation care, per day, for the evaluation and management of a patient, which requires a medically appropriate history and/or examination and straightforward or low level medical decision making. When using total time on the date of the encounter for code selection, 40 minutes must be met or exceeded. |
| 99222 | Initial hospital inpatient or observation care, per day, for the evaluation and management of a patient, which requires a medically appropriate history and/or examination and moderate level of medical decision making. When using total time on the date of the encounter for code selection, 55 minutes must be met or exceeded. |
| 99223 | Initial hospital inpatient or observation care, per day, for the evaluation and management of a patient, which requires a medically appropriate history and/or examination and high level of medical decision making. When using total time on the date of the encounter for code selection, 75 minutes must be met or exceeded. |
| 99234 | Hospital inpatient or observation care, for the evaluation and management of a patient including admission and discharge on the same date, which requires a medically appropriate history and/or examination and straightforward or low level of medical decision making. When using total time on the date of the encounter for code selection, 45 minutes must be met or exceeded. |
| E0780 | Ambulatory infusion pump, mechanical, reusable, for infusion less than 8 hours |
| J1412 | Injection, valoctocogene roxaparvovec-rvox, per ml, containing nominal 2 x 10^13 vector genomes |
| ICD-10 codes considered medically necessary if criteria are met: | |
| *Code* | *Description* |
| D66 | Hereditary factor VIII deficiency |

## References


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## Clinical Guideline Revision / History Information

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