Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

P&T Date: 08/07/2025

Roctavian™ (valoctocogene roxaparvovec)

HCPCS: J1412

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved age
   b. Diagnosis of severe hemophilia A with factor VIII level < 1% IU/dL
   c. Must not have detectable pre-existing immunity to the adeno-associated virus serotype 5 (AAV5) capsid
   d. Must not have a history of inhibitors to factor VIII or a positive factor VIII inhibitor screen defined as greater than or equal to 0.6 Bethesda units prior to administration of Roctavian
   e. Must have been treated with or exposed to factor VIII concentrates or cryoprecipitate for a minimum of 150 exposure days
   f. Must be treatment experienced with Hemlibra® for at least 6 months and experienced treatment failure defined as any of the following:
      i. Spontaneous soft tissue bleeding event
      ii. Micro-bleeding into a joint
      iii. Ongoing joint pain of a known target joint
   g. Must not have received prior treatment with any gene therapy for hemophilia A or are being considered for treatment with any other gene therapy for hemophilia A
   h. Must be being treated at a federally recognized hemophilia treatment center site
   i. The requesting physician attests to providing clinical outcome information within the appropriate provider portal as requested by BCBSM
   j. Trial and failure, contraindication, or intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list.

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: 3 months
   c. Renewal Criteria: Not applicable as no further authorization will be provided

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Roctavian is an adeno-associated virus vector-based gene therapy indicated for the treatment of adults with severe hemophilia A without antibodies to adeno-associated virus serotype 5 (AAV5).

- Hemophilia A is a rare genetic bleeding disorder in which affected individuals have insufficient levels of factor VIII. It is the second most common type of hemophilia and caused by mutations in the F8 gene. The F8 gene is located on the X chromosome and thus the disease is inherited as an X-linked recessive trait. About 30% of cases are the result of spontaneous genetic mutations. Overall incidence is estimated at 1 in 5,000 male births.

- The symptoms and severity of hemophilia A may vary greatly from one person to another. Hemophilia A can range from mild to moderate to severe.

    - Mild hemophilia patients have a factor activity of 5% to 40% and usually do not experience any major problems in everyday life. It often goes unnoticed until puberty or adulthood when bleeding after surgery or a deep cut lasts longer than normal. These patients do not typically need prophylactic therapy and only require on-demand factor for injuries or surgeries.

    - Moderate hemophilia patients have a factor activity of 1% to 5% and may have occasional episodes of spontaneous bleeding from deep tissues such as joints and muscles. These episodes are usually associated with some injury or inciting event. Individuals with moderate hemophilia A are at risk for prolonged bleeding following surgery or trauma. Affected individuals are usually diagnosed by 5 or 6 years of age. The frequency of spontaneous bleeding episodes in individuals with moderate hemophilia A is highly variable resulting in some patients needing consistent prophylactic factor VIII and others only needing on-demand factor VIII for medical procedures.

    - Severe hemophilia patients have a factor level of less than 1% and often have bleeding for no known reason, especially in the joints and muscles. From infancy, patients bruise easily and as they become more active, learn to walk, and put more strain on their joints and muscles, bleeding starts to occur. Without preventative treatment, a young child may experience 2 to 5 spontaneous bleeding episodes per month.

- Hemophilia A should be suspected in individuals presenting with a history of easy bruising, spontaneous bleeding, particularly into the joints, muscles, and soft tissues, or excessive bleeding following trauma or surgery. If hemophilia is suspected, the clinician should obtain the patient's bleeding history and family history of abnormal or unexplained bleeding experienced by any siblings or maternal male relatives to assess patterns of inheritance and assist with diagnosis. A definitive hemophilia A diagnosis is based on a factor assay to demonstrate a deficiency of factor VIII. Once an individual is diagnosed with hemophilia A, the specific mutation in the F8 gene responsible for causing hemophilia may be identified.

- The current standard of care for hemophilia A is the use of factor VIII replacement therapy. There are two types of factor products available to treat hemophilia which include plasma derived factor, entirely made of plasma from human donations and recombinant factor, which is made by genetically engineered technology, both with standard and extended half-life products. All factor products have demonstrated to have similar safety and efficacy in clinical studies treating or reducing bleeding episodes with the apparent difference in the frequency of administration: up to three times weekly injections for standard products and weekly or every two weeks for extended half-life products.

To be enrolled in the GENEr8-1 trial, patients needed to be stable on factor VIII therapy for 12 months prior Roctavian administration.

- Hemlibra (emicizumab) is a recombinant, humanized, bispecific monoclonal antibody that bridges activated factor IX and factor X to restore the function of missing activated factor VIII in hemophilia A patients to restore hemostasis. It can be used to treat patients without inhibitors who continue having spontaneous bleeds on prophylactic factor VIII therapy. Failure of Hemlibra is denoted by spontaneous soft tissue bleeds, micro-bleeding into a joint, or ongoing joint pain of a known target joint.

- It is estimated that up to 30% of individuals with severe hemophilia A develop inhibitors against factor VIII replacement therapy. Inhibitors most often develop during childhood, especially during the first 20 exposure days. Exposure days are counted as a day during which a patient receives factor. Controlling bleeds is a greater challenge in hemophilia patients with inhibitors than in those without. Inhibitors to factor VIII are associated with a higher disease burden, including increased risk of musculoskeletal complications, pain, physical limitations, and treatment challenges, all of which may impact a patient's physical functioning, capacity for physical activities, and quality of life. The definition of a positive inhibitor is a Bethesda titer of greater than or equal to 0.6 BU for factor VIII. Patients positive for factor VIII inhibitors or with a prior history of factor VIII inhibitors were excluded from the GENEr8-1 trial. In order to limit the risk of inhibitor development following Roctavian therapy, the GENEr8-1 study also required patients had greater than 150 prior exposure days to factor IX therapy before receiving gene therapy.

- Roctavian uses an AAV5 vector to deliver a functional copy of the F8 gene to the patient's liver where functional factor VIII is produced. Patients with high AAV5 antibody titers may not respond to gene therapy due to the antibodies neutralizing Roctavian before the functional F8 gene can be properly incorporated into the patient's genome. The GENEr8-1 study excluded patients from the trial based on antibody titers and is only indicated in those without AAV5 antibodies.

- Roctavian has not been studied and there is no data to support use in combination with other gene therapies indicated for use in hemophilia A.

- A provider portal is used to capture clinical outcome information for patients on select high-cost treatments, such as gene and cellular therapies. If a patient meets medical necessity as defined by this policy and is approved for treatment, the requesting physician must attest to providing clinical outcome information within the appropriate provider portal at the requested cadence.

References:

1. Roctavian [prescribing information]. Novato, CA: BioMarin Pharmaceutical Inc.; June 2023.
2. Clinicaltrials.gov. Study to evaluate the efficacy and safety of valoctocogene roxaparvovec, with prophylactic steroids in hemophilia A (GENEr8-3) (NCT04323098). Available at: https://classic.clinicaltrials.gov/ct2/show/NCT04323098. Accessed on June 30, 2023.
3. Ozelo MC, Mahlangu J, Pasi KJ, et al. Valoctocogene roxaparvovec gene therapy for hemophilia A. NEJM. 2022 March 17; 386: 1013 – 25.
4. National Organization for Rare Disorders. Hemophilia A. 2022 Aug 31. Available at: https://rarediseases.org/rare-diseases/hemophilia-a/?filter=ovr-ds-resources. Accessed on July 5, 2023.
5. World Federation of Hemophilia. Guidelines for the management of hemophilia. Haemophilia. 2020 August 3. Available at: https://onlinelibrary.wiley.com/doi/epdf/10.1111/hae.14046. Accessed on: July 5, 2023.

<table>
<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>1.9</td><td>Effective Date: 08/07/2025</td><td>Updated the provider portal from Audaire to the appropriate provider portal</td></tr>
<tr><td>1.8</td><td>Effective Date: 08/08/2024</td><td>Annual review of criteria was performed, no changes were made</td></tr>
<tr><td>1.7</td><td>Effective Date: 08/10/2023</td><td>New policy. This criteria replaces previously approved preliminary criteria</td></tr>
<tr><td>1.6</td><td>Effective Date: 07/10/2023</td><td>UM medical management system update for MAPPO and BCNA
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table></td></tr>
<tr><td>1.5</td><td>Effective Date: 07/06/2023</td><td>UM medical management system update for BCBS and BCN
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table></td></tr>
<tr><td>1.4</td><td>Effective Date: 04/06/2023</td><td>Annual review of criteria was performed, no changes were made</td></tr>
<tr><td>1.3</td><td>Effective Date: 04/14/2022</td><td>Annual review of criteria was performed, no changes were made</td></tr>
<tr><td>1.2</td><td>Effective Date: 04/08/2021</td><td>Annual review of criteria was performed, no changes were made</td></tr>
<tr><td>1.1</td><td>Effective Date: 04/16/2020</td><td>Criteria Update</td></tr>
<tr><td>1.0</td><td>Effective Date: 08/15/2019</td><td>Preliminary Drug Review
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>No</td></tr><tr><td>BCN</td><td>No</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table></td></tr>
</table>

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*

Blue Cross Blue Shield/Blue Care Network of Michigan
Medication Authorization Request Form
Roctavian (valoctocogene roxaparvovec)
HCPCS CODE: J1412

Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

This form is to be used by participating physicians to obtain coverage for Roctavian. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

PATIENT INFORMATION		PHYSICIAN INFORMATION
Name		**Name**
ID Number		**Specialty**
D.O.B.	☐ Male ☐ Female	**Address**
Diagnosis		**City /State/Zip**
Drug Name	☐ Roctvian	**Phone/Fax: P**: ( ) - **F**: ( ) -
Dose and Quantity		**NPI**
Directions		**Contact Person**
Date of Service(s)		**Contact Person Phone / Ext.**

STEP 1: DISEASE STATE INFORMATION

1. Is this request for: ☐ Initiation ☐ Continuation of therapy *Date when patient start therapy*: _____

2. Please provide the NPI number for the place of administration: _____

3. Please specify the location of administration (e.g. name of facility): _____

4. Has the clinical outcome information been provided within the Audaire Health provider portal as requested by BCBSM?
   ☐ Yes ☐ No Comment _____

5. **Initiation AND Continuation of therapy:**
   a. Is the patient diagnosed with hemophilia A WITH factor VIII deficiency? ☐ Yes ☐ No, please specify: _____
      i. Please indicate how the patient's hemophilia is classified:
      ☐ Mild hemophilia (factor VIII level of 6% - 40%)
      ☐ Moderate hemophilia (factor VIII level of 1% - 5%)
      ☐ Severe hemophilia (factor VIII level < 1%)
      ☐ Unknown
   b. Does the patient have pre-existing immunity to adeno-associated virus serotype 5 (AAV5) capsid? ☐ Yes ☐ No
   c. Does the patient have a history of inhibitors to factor VIII or a positive factor VIII inhibitor screen prior to administration of Roctavian?
      ☐ Yes, please specify level: _____ ☐ No
   d. Has the patient been treated with or exposed to factor VIII concentrates or cryoprecipitate for a minimum of 150 exposure day?
      ☐ Yes ☐ No
   e. Has the patient experienced treatment failure with Hemlibra in the past 6 months?
      ☐ No, please specify: _____
      ☐ Yes, please provide patient's response to Hemlibra below:
      ☐ Spontaneous soft tissue bleeding event
      ☐ Micro-bleeding into a joint
      ☐ Ongoing joint pain of a known target joint
      ☐ Other: _____
   f. Has the patient been treated with any gene therapy or being considered for treatment with gene therapy for hemophilia A?
      ☐ Yes ☐ No
   g. Is Roctavian being dispensed by a treatment center associated with hemophilia that provides high quality hemophilia care with outcome-based results (ie: hemophilia treatment center)? ☐ Yes ☐ No

6. **Continuation of therapy -** *Please include rationale for continuation of therapy*_____

7. *Please add any other supporting medical information necessary for our review*

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name **Physician Signature** **Date**

Step 2: Checklist	☐ Form Completely Filled Out ☐ Attached necessary chart notes	☐ Important laboratory results
Step 3: Submit	**By Fax: BCBSM Specialty Pharmacy Mailbox** **1-877-325-5979**	**By Mail: BCBSM Specialty Pharmacy Program** **P.O. Box 312320, Detroit, MI 48231-2320**