09-J4000-62

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Subject: Valoctocogene Roxaparvovec-rvox (Roctavian)

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Dosage/ Administration | Position Statement | Billing/Coding | Reimbursement | Program Exceptions | Definitions

Related Guidelines | Other | References | Updates

DESCRIPTION:

Valoctocogene roxaparvovec-rvox (Roctavian), an adeno-associated virus (AAV) vector–based gene therapy, was approved by the U.S. Food and Drug Administration (FDA) in 2023 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. This is the first FDA-approved gene therapy for this indication. Valoctocogene roxaparvovec-rvox is a one-time intravenous infusion, which delivers a functional copy of the human Factor VIII (hFVIII) gene into target liver cells, enabling patients to endogenously synthesize their own therapeutic FVIII protein.

The safety and efficacy of valoctocogene roxaparvovec-rvox were evaluated in an open-label, single arm study of adult males with hemophilia A and FVIII levels of less than or equal to 1% of normal (GENEr8-1, NCT03370913). Subjects were required to have received prophylaxis therapy and have at least 150 previous exposure days of treatment with FVIII protein. Patients with a history of FVIII inhibitors, active infection with hepatitis B or C, or prior gene therapy were excluded. All subjects received a single intravenous dose of 6×10^{13} vector genomes per kg body weight of valoctocogene roxaparvovec-rvox (n=134). The primary efficacy outcome for the analysis was a non-inferiority evaluation of the difference in ABR during the post-treatment evaluation period compared with baseline.

The following table summarizes the noninferiority comparison between the mean ABR after valoctocogene roxaparvovec-rvox therapy and the mean baseline ABR while patients were on factor VIII prophylaxis in the rollover population (N=112).

ABR and Bleeding Events	Baseline	Post-Valoctocogene roxaparvovec-rvox Efficacy Evaluation Period
Median (range) follow-up duration in years	0.6 (0.5, 1.3)	3.0 (1.7, 3.7)
Follow-up duration in person-years	78.3	342.8
Mean (SD) ABR in bleeds/year	5.4 (6.9)	2.6 (6.2)*
Median (min, max) ABR in bleeds/year	3.3 (0, 34.6)	0.3 (0, 35.0)*
Observed spontaneous bleed count (proportion of total bleeds)	176 (42%)	179 (41%)
Observed joint bleed count (proportion of total bleeds)	240 (57%)	195 (45%)

Min: Minimum; Max: Maximum; SD: Standard Deviation

*A total of 13 patients (12%) had used factor VIII replacement products or emicizumab during the efficacy evaluation period for prophylaxis, with a median start time at 2.3 (range, 0.1 to 3.3) years. An ABR of 35 was imputed for the periods when these patients were on prophylaxis.

In the rollover population, a total of 5 patients (4%) did not respond and 17 patients (15%) lost response to valoctocogene roxaparvovec-rvox therapy over a median time of 2.3 (range: 1.0 to 3.3) years. In the directly enrolled population with a longer follow-up, a total of 1 patient (5%) did not respond and 6 patients (27%) lost response to valoctocogene roxaparvovec-rvox treatment over a median time of 3.6 (range, 1.2 to 4.3) years. The most common adverse reactions were mild changes in liver function, headache, nausea, vomiting, fatigue, abdominal pain, and infusion-related reactions.

POSITION STATEMENT:

Valoctocogene roxaparvovec-rvox (Roctavian) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with hemophilia A
2. Member's endogenous factor VIII is less than or equal to 1 IU/dL (1%) – laboratory documentation must be provided
3. Member has been seen by a board-certified hematologist-oncologist or hematologist in the past 12 months – documentation from medical record must be provided, including ALL of the following:
    a. Complete hematologic and musculoskeletal assessment

   b. Factor replacement protocol (including dosing for both acute and prophylactic management)
   c. Treatment log documenting any bleeds and required treatment within the past 12 months
4. Member does not have inhibitors to factor VIII
5. Member does not have antibodies to adeno-associated virus serotype 5 (AAV5) – laboratory documentation must be provided
6. The member does NOT have significant liver dysfunction as defined by abnormal elevation of any of the following – laboratory documentation within the past 3 months must be provided:
   a. ALT (alanine transaminase) 3 times the upper limit of normal
   b. Bilirubin above 3 times the upper limit of normal
   c. Alkaline phosphatase above 3 times the upper limit of normal
   d. INR (international normalized ratio) greater than or equal to 1.4
7. Member has had clinically evident bleeding (defined as: 1 or more episodes of spontaneous bleeding into a joint or into the central nervous system; or 4 or more episodes of soft tissue bleeding in an 8-week period) after a two-month trial of at least one factor VIII prophylaxis product
8. Member was previously approved by Florida Blue for a factor VIII prophylaxis product
9. Member does not have a history of prior gene therapy use (including prior treatment with valoctocogene roxaparvovec-rvox)
10. Valoctocogene roxaparvovec-rvox is prescribed by a board-certified hematologist or hematologist-oncologist
11. Member is at least 18 years of age

Approval duration: 6 months (1 lifetime treatment)

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Can be administered only once

Dose Adjustments

- None

Drug Availability

- Suspension for intravenous infusion

- Nominal concentration of 2 × 1013 vg valoctocogene roxaparvovec-rvox per mL, each vial contains an extractable volume of not less than 8 mL (16 × 1013 vg)

Boxed Warning

- None

Contraindications

- None

Precautions/Warnings

- Infusion-related reactions: Infusion reactions, including hypersensitivity reactions and anaphylaxis, have occurred
- 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).
- Monitoring laboratory tests: Monitor for factor VIII activity and factor VIII inhibitors.
- 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. In the event that any malignancy occurs after treatment.

BILLING/CODING INFORMATION:

HCPCS Coding

J3590	Unclassified biological

ICD-10 Diagnosis Codes That Support Medical Necessity

D66	Hereditary factor VIII deficiency

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None

RELATED GUIDELINES:

Clotting Factors and Coagulant Drug Products, 09-J0000-34

OTHER:

None

REFERENCES:

1. BioMarin. Roctavian (valoctocogene roxaparvovec-rvox) injection, solution. 2023 [cited 2/29/24]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=0dcf7185-8e1c-456a-9d4e-7cc316400118
2. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2024 [cited 2/29/24]. Available from: http://www.clinicalpharmacology.com/.
3. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2000 Feb 29 - [cited 2/29/24]. Available from: http://clinicaltrials.gov/.
4. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 2/29/24]. Available online.
5. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2024 [cited 2/29/24]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 03/13/24.

GUIDELINE UPDATE INFORMATION:

04/01/24	New Medical Coverage Guideline.