ROCTAVIAN®
(valoctocogene roxaparvovec-rvox)
Suspension for intravenous infusion

ROCTAVIAN® Laboratory Support Program Healthcare Provider Frequently Asked Questions

The ROCTAVIAN® Laboratory Support Program, in partnership with Quest Diagnostics, offers pre-infusion eligibility and post-infusion follow-up testing at no cost to eligible, commercially insured adults with severe hemophilia A.*

Click on each section below to learn more.

Program Overview

Enrollment and Scheduling

Test Results and Lab Information

Contact Information

*Terms and Conditions apply. Valid only for patients with commercial prescription insurance coverage who have a valid prescription for an FDA-approved indication and who meet additional eligibility criteria. Not valid for prescriptions reimbursed, in whole or in part, by any federal, state, or government-funded insurance programs (for example, Medicare, Medicare Advantage, Medigap, Medicaid, VA, DoD, or TRICARE) or where prohibited by law or by the patient's health insurance provider. If at any time a patient begins receiving prescription drug coverage under any federal, state, or government-funded healthcare program, the patient will no longer be able to use the program and patient must notify BioMarin RareConnections at 1-866-906-6100 to stop participation. Patients residing in or receiving treatment in certain states may not be eligible for some or all of the program elements. Patients may not seek reimbursement for value received from the program from any third-party payers. Additional restrictions may apply. Offer subject to change or discontinuance without notice. This assistance offer is not health insurance. See **BioMarin-copay-terms.com** for full Terms and Conditions.

Please see Important Safety Information on the following pages.

Indication and Important Safety Information

ROCTAVIAN® (valoctocogene roxaparvovec-rvox) is 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 detected by an FDA-approved test.

Contraindications: Patients with active infections, either acute (such as acute respiratory infections or acute hepatitis) or uncontrolled chronic (such as chronic active hepatitis B). Patients with known significant hepatic fibrosis (stage 3 or 4 on the Batts-Ludwig scale or equivalent), or cirrhosis, and patients with known hypersensitivity to mannitol.

Infusion-related reactions including hypersensitivity reactions and anaphylaxis, have occurred. Monitor during and for at least 3 hours after ROCTAVIAN administration. Administer ROCTAVIAN in a setting where personnel and equipment are immediately available to treat infusion-related reactions. Discontinue infusion for anaphylaxis.

Hepatotoxicity: The safety and effectiveness of ROCTAVIAN in patients with hepatic impairment has not been established. Perform liver health assessments prior to administration. The majority of patients treated with ROCTAVIAN experienced ALT elevations and required corticosteroids for ALT elevation. Assess patient's ability to receive corticosteroids and/or other immunosuppressive therapy that may be required for an extended period. Live vaccines should not be administered to patients while on immunosuppressive therapy.

Monitor ALT weekly for at least 26 weeks and as clinically indicated, during corticosteroid therapy 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. One case of autoimmune hepatitis was reported during third year follow-up in a patient with history of hepatitis C and steatohepatitis.

It is recommended that patients abstain from consuming alcohol for at least 1 year after administration and thereafter limit alcohol use. Concomitant medications may cause hepatotoxicity, decrease Factor VIII activity, or change plasma corticosteroid levels which may impact liver enzyme elevation and/or Factor VIII activity or

decrease the efficacy of the corticosteroid regimen or increase their side effects. Closely monitor concomitant medication use including herbal products and nutritional supplements and consider alternative medications in case of potential drug interactions.

Thromboembolic Events: Factor VIII activity above ULN has been reported following ROCTAVIAN® infusion. Thromboembolic events may occur in the setting of elevated Factor VIII activity above ULN. Evaluate patients for risk of thrombosis including general cardiovascular risk factors before and after administration of ROCTAVIAN. Advise patients on their individual risk of thrombosis in relation to their Factor VIII activity levels above ULN and consider prophylactic anticoagulation. Advise patients to seek immediate medical attention for signs or symptoms indicative of a thrombotic event.

Factor VIII Inhibitors and Monitoring for Inhibitors. The safety and effectiveness of ROCTAVIAN in patients with prior or active Factor VIII inhibitors have not been established. Patients with active Factor VIII inhibitors should not take ROCTAVIAN. Following administration, monitor patients for Factor VIII inhibitors (neutralizing antibodies to Factor VIII). Test for Factor VIII inhibitors especially if bleeding is not controlled, or plasma Factor VIII activity levels decrease.

Monitor Factor VIII using the same schedule for ALT monitoring. It may take several weeks after ROCTAVIAN infusion before ROCTAVIAN-derived Factor VIII activity rises to a level sufficient for prevention of spontaneous bleeding episodes. Exogenous Factor VIII or other hemostatic products may also be required in case of surgery, invasive procedures, trauma, or bleeds.

Consider more frequent monitoring in patients with Factor VIII activity levels ≤5 IU/dL and evidence of bleeding, taking into account the stability of Factor VIII levels since the previous measurement.

Factor VIII activity produced by ROCTAVIAN in human plasma is higher if measured with one-stage clotting assays compared to chromogenic substrate assays. When switching from hemostatic products prior to ROCTAVIAN treatment, physicians should refer to the relevant prescribing information to avoid the potential for Factor VIII activity assay interference during the transition period.

Malignancy: The integration of liver-targeting AAV vector DNA into the genome may carry the theoretical risk of hepatocellular carcinoma development. ROCTAVIAN can also insert into the DNA of other human body cells. Monitor patients with risk factors for hepatocellular carcinoma (eg, hepatitis B or C, nonalcoholic fatty liver disease, chronic alcohol consumption, nonalcoholic steatohepatitis, advanced age) with regular liver ultrasound (eg, annually) and alpha-fetoprotein testing for 5 years following ROCTAVIAN administration. In the event that any malignancy occurs after treatment with ROCTAVIAN, contact BioMarin Pharmaceutical Inc. at 1-866-906-6100.

Most Common Adverse Reactions: Most common adverse reactions (incidence ≥5%) were nausea, fatigue, headache, infusion-related reactions, vomiting, and abdominal pain. Most common laboratory abnormalities (incidence ≥10%) were ALT, AST, LDH, CPK, Factor VIII activity levels, GGT, and bilirubin >ULN. Patients also experienced adverse reactions from corticosteroid use.

Isotretinoin, Efavirenz, and HIV-Positive Patients. Isotretinoin is not recommended in patients who are benefiting from ROCTAVIAN. Efavirenz is not recommended in patients treated with ROCTAVIAN. Clinical studies of ROCTAVIAN did not include sufficient numbers of patients with HIV to determine whether the efficacy and safety differs compared to patients without HIV infection.

Females and Males of Reproductive Potential. ROCTAVIAN is not intended for administration in women. There are no data on the use of ROCTAVIAN in pregnant women or regarding lactation. For 6 months after administration of ROCTAVIAN, men of reproductive potential and their female partners must prevent or postpone pregnancy using an effective form of contraception, and men must not donate semen.

You may report side effects to the FDA at 1-800-FDA-1088 or **www.fda.gov/medwatch**. You may also report side effects to BioMarin Pharmaceutical Inc. at 1-866-906-6100.

Please see additional safety information in the Prescribing Information**.**

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