

# TAKE THE FIRST STEPS TO TREATMENT



## Determining eligibility for ROCTAVIAN

The only one-time gene therapy indicated for the treatment of adults with severe hemophilia A<sup>1</sup>

### Indication and Important Safety Information

ROCTAVIAN 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.

Please see Important Safety Information throughout and in the Prescribing Information.

# Patient eligibility starts with you<sup>1</sup>

## The following eligibility criteria must be met before a patient can be considered for ROCTAVIAN:

-  **Adult** ( $\geq 18$  years of age)
-  **Severe hemophilia A** (congenital Factor VIII deficiency with Factor VIII activity  $\leq 1$  IU/dL)
-  **No active inhibitors** to Factor VIII
-  **No active infections**, either acute (such as acute respiratory infections or acute hepatitis) or uncontrolled chronic (such as chronic active hepatitis B), or known hypersensitivity to mannitol
-  **No known significant hepatic fibrosis or cirrhosis** as determined by a baseline assessment of liver health (liver function tests, ultrasound and elastography or laboratory assessments for liver fibrosis)
-  **No antibodies to AAV5**  
AAV5 DetectCDx™ is a prescription-only companion diagnostic blood test that detects antibodies to AAV5

## Review clinical requirements and lifestyle considerations prior to prescribing ROCTAVIAN

### Safety Considerations

- Patients should be evaluated before and after administration of ROCTAVIAN for risk factors for **thrombosis** and general cardiovascular risk factors<sup>1</sup>
- 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<sup>1</sup>
- The majority of patients treated with ROCTAVIAN experienced ALT elevations and required **corticosteroids**. Assess patient's ability to receive corticosteroids and/or other immunosuppressive therapy that may be required for an extended period<sup>1</sup>

### Lifestyle Considerations

- It is recommended that patients abstain from consuming **alcohol** for at least 1 year after administration of ROCTAVIAN, and thereafter limit alcohol use<sup>1</sup>
- For 6 months after receiving 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**<sup>1</sup>

AAV5 DetectCDx™ is a trademark of ARUP Laboratories.

Please see Important Safety Information throughout and in the [Prescribing Information](#).

# Steps to treatment

Take the first steps to treatment. Test your patients to confirm eligibility, and assess if ROCTAVIAN gene therapy is right for them.

STEP

1

## Conduct required eligibility testing:

- Bloodwork (AAV5 DetectCDx™, liver function tests, Factor VIII inhibitor titer test)
- Liver ultrasound and elastography or laboratory assessments for assessing hepatic fibrosis

Visit [biomarin-rareconnections.com](http://biomarin-rareconnections.com) to see if your patient is eligible for financial support services.

STEP

2

## Discuss lifestyle, monitoring, and safety considerations with your patients.

Confirm the decision to treat with ROCTAVIAN.

STEP

3

Fill out the **Patient Enrollment Form** to initiate the prescription for ROCTAVIAN.

Test and assess your patients for eligibility today

## Important Safety Information (cont.)

**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.

**Please see Important Safety Information throughout and in the Prescribing Information.**

**ROCTAVIAN™**  
(valoctocogene roxaparvovec-rvox)  
Suspension for intravenous infusion

# Indication and Important Safety Information

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**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.

# Important Safety Information (cont.)

**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  $\leq 5$  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  $\geq 5\%$ ) were nausea, fatigue, headache, infusion-related reactions, vomiting, and abdominal pain. Most common laboratory abnormalities (incidence  $\geq 10\%$ ) 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](http://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.**

# BioMarin RareConnections™ Support Program



## A one-time ROCTAVIAN gene therapy. Personalized product and education support.

BioMarin RareConnections provides patients and HTCs with personalized product support throughout the ROCTAVIAN journey:

- Understanding and accessing eligibility tests
- Identification of financial programs for commercially insured patients, such as co-pay assistance\* for eligibility testing and post-infusion monitoring
- Education on payer requirements needed to access treatment
- Coordination for product shipment



To learn more about how BioMarin RareConnections can help your patients, visit our website at [BioMarin-RareConnections.com](https://www.BioMarin-RareConnections.com).

\*Valid only for those patients with commercial prescription insurance coverage for products who meet eligibility criteria. Offer not valid for prescriptions, administration, or related labs 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), for cash-paying patients, where product, administration, or related lab, are not covered by patient's commercial insurance, where patient's commercial insurance plan reimburses them for the entire cost of their prescription drug, administration, and/or related labs, or where prohibited by law or by the patient's health insurance provider. Patients who are residents of certain states (MA or RI) are not eligible for drug administration co-pay support. Patients who are residents of certain states (MI, MN, or RI) are not eligible for laboratory services co-pay support. If at any time a patient begins receiving prescription drug, administration, or related lab coverage under any such federal, state, or government-funded healthcare program, patient will no longer be able to use the BioMarin Co-Pay Assistance Program and patient must notify BioMarin RareConnections™ at 1-833-ROCTAVIAN (1-833-762-8284) to stop participation. Patients may not seek reimbursement for the value of the out-of-pocket expense amount covered by the Program from any third-party payer, whether public or private. The Program is valid ONLY for qualifying patients residing in the 50 U.S. states or in Puerto Rico with commercial insurance who have a valid prescription for an FDA-approved indication for the qualifying BioMarin therapy. This program is not health insurance. Offer may not be combined with any other rebate, coupon, or offer. Co-payment assistance under the Program is not transferable. BioMarin Pharmaceutical Inc. reserves the right to rescind, revoke, or amend the Program without notice. Patient/caregiver certifies responsibility for complying with applicable limitations, if any, of any commercial insurance and reporting receipt of program rewards, if necessary, to any commercial insurer. The Program is subject to termination or modification at any time. Some restrictions apply.

**Reference:** 1. ROCTAVIAN™ (valoctocogene roxaparovec-rvox). Prescribing information. BioMarin Pharmaceutical Inc. 2023.

**Please see Important Safety Information throughout and in the Prescribing Information.**

BIOMARIN

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 **ROCTAVIAN™**  
(valoctocogene roxaparovec-rvox)  
Suspension for intravenous infusion