Pharmacy Focus:
Roctavian™ — Long-Awaited Gene Therapy for Hemophilia A

Key Takeaways

- Roctavian is the first gene therapy approved for adults with severe hemophilia A who do not have antibodies to the viral vector used for Roctavian.
- This gene therapy offers a one-time, single-dose infusion to potentially increase factor VIII levels to reduce both bleeding episodes and the need for prophylactic therapy.
- The projected estimated cost of Roctavian is $2,900,000 for the one-time infusion.

Hemophilia A Disease Overview[1-3]

Hemophilia is a rare disorder characterized by excessive bleeding due to impaired blood clotting. Those with hemophilia most commonly present with unusual bruising and bleeding, which can be both external or internal. Excessive bleeding can occur with cuts or scrapes, dental work and surgeries. However, with more severe cases, bleeds can appear spontaneously. Larger joints, such as knees, ankles and elbows, are most affected.

There are different types of hemophilia, including hemophilia A, hemophilia B, and von Willebrand disease (only hemophilia A will be covered in this document). It is estimated more than around 33,000 people in the U.S. have hemophilia, the majority having hemophilia A, which is caused by decreased or absent levels of clotting factor VIII. Patients with hemophilia may have mild, moderate or severe disease based on their factor VIII levels. Severe disease is estimated to account for about 60% of hemophilia A patients.

Hemophilia A is much more common in males than females. The disease is the most common in non-Hispanic white males. Generally, those with severe disease are often diagnosed within a month of birth. Meanwhile, mild hemophilia is diagnosed at around 36 months of age.

Current Treatment Options[4-6]

The current standard of care treatment for those with hemophilia A is the replacement of factor VIII clotting protein to prevent bleeding episodes and other complications. Factor replacement products can be derived from human blood/plasma or be recombinant (manufactured in a laboratory with no human blood proteins). Recombinant factor replacement products are favored, as they have no risk of virus transmission.

Complications of factor replacement therapy can include infusion reactions and the development of inhibitors. Inhibitors prevent the current factor treatments from working the same as before, making it more difficult to prevent or stop a bleeding episode. The presence of inhibitors requires the use of increased doses and can end up costing more than $1.5 million per year, versus $500,000 to $1,100,000 for severe patients without inhibitors.

Hemlibra® (emicizumab-kxwh), a monoclonal antibody, is also available as a prophylactic treatment approved for all ages (newborns and older) with hemophilia A with or without factor VIII inhibitors.

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	Factor VIII Replacement Products (e.g., Advate®, Hemofil M®, Kogenate FS®, etc.)	**Hemlibra®**	**Roctavian™**
FDA-Approved Use	**For children and adults for:** • On-demand treatment and control of bleeding episodes • Perioperative management of bleeding • Routine prophylaxis	**For children and adults for:** • Routine prophylaxis • With or without factor VIII inhibitors	**For adults with:** • Severe hemophilia (factor VIII levels <1 IU/dL) • No history of antibiodies to viral vector used to deliver gene therapy
Average Annual Cost	$700,000*	$750,000*	$2,900,000 (once)[7]
Payment Structures	Medical and/or Prescription Benefits	Medical and/or Prescription Benefits	Medical Benefits
HCPCS Codes for Medical Billing	J7190-J7192, J7188, J7182	J7170	C9399, J3590

**Average cost for factor VIII replacement products seen in HM Insurance Group cases (2021-2023).*

Roctavian Overview[8-12]

Roctavian (valoctocogene roxaparvovec-rvox) is a new gene therapy produced by BioMarin. It was approved by the FDA on June 30, 2023, for adults with severe hemophilia A (levels of factor VIII <1 IU/dL) who do not have antibodies to the viral vector used to deliver the gene therapy. There is a low likelihood of use in patients with confirmed inhibitors as well as comorbidities that can include active or uncontrolled chronic infection, liver disease (i.e., hepatitis, cirrhosis, etc.), thromboembolic events and unrelated bleeding disorders.

Overall, the goal of the one-time Roctavian infusion is to increase the production of factor VIII clotting factor to reduce both bleeding episodes and the need for prophylactic and/or as needed factor replacement therapy. The path to approval, however, has been long for Roctavian, starting back in 2020 when the FDA requested additional long-term data to show the potential durability of this gene therapy.

For the approval, BioMarin provided three-year results from the largest and longest phase III study for hemophilia — the GENEr8-1 study — that included 134 participants. Results from the study showed a 52% decrease in the annualized bleeding rate (2.6 bleeds per year versus 5.4 bleeds per year at baseline). The majority of participants did not restart prophylaxis by the end of year three; however, six patients did need to be reinitiated on factor VIII prophylaxis, and one participant restarted prophylaxis with Hemlibra.

Roctavian's onset of action is long, so factor VIII prophylaxis continued until after week four post-infusion in the clinical trial. Corticosteroids will likely be added as pre-treatment protocols to decrease the chance of adverse effects. It is also important to note that response to Roctavian may decrease over time, as beyond year two, most participants' factor VIII levels had dropped to that of mild to moderate hemophilia. A long-term study is planned by BioMarin that will continue to follow the participants in the GENEr8-1 study for up to 15 years.

BioMarin has stated that an outcomes-based warranty will be available to payers. This warranty includes 100% of the cost if the patient does not respond at all to therapy with Roctavian or a prorated reimbursement through the first four years of treatment if response is lost.

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Cost Containment Considerations

As part of its HMConnects™ cost containment program, HM Insurance Group (HM) works to support cost-management opportunities around the use of gene and cell therapies and other high-cost pharmaceutical treatment options that can impact our clients' bottom lines. The Pharmacy Operations (RxOps) team watches the market — and our book of business — to anticipate how current and future advancements may impact financial risk levels for HM's client base. Standard practices include reviewing, auditing and collaborating on the content of current policies, monitoring trends and implementing appropriate cost-savings techniques. Additional practices include the prevention of stockpiling, working to ensure prescriptions are filled via in-network pharmacies and assessing to determine if patients are properly dosed based on weight and lab values when appropriate. All of these services are provided to HM's clients at no additional cost to them.

Pharmacy Focus provides valuable information about pharmaceutical industry developments and their associated costs that can impact the growing claims trend in the self-funded insurance market. Be aware of influences and gain insight into approaches that may help to contain costs. Please share topic suggestions or feedback with **HMPharmacyServices@hmig.com**.

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