Pharmacy Focus:
Current and Upcoming Hemophilia Treatment

Hemophilia Overview

Hemophilia is a rare genetic disorder characterized by excessive bleeding due to impaired blood clotting. Those with hemophilia most commonly present with unusual bruising and bleeding. Excessive bleeding can occur with cuts or scrapes, dental work and surgeries. However, with more severe cases, bleeds can occur spontaneously. Along with external bleeds, internal bleeds may occur. Larger joints, such as knees, ankles and elbows, are most commonly affected.[1]

Types of Hemophilia (*most prevalent*)**:**

Type	Details	ICD-10 Code
Hemophilia A	Caused by decreased or absent levels of **clotting factor VIII**; the most common type of hemophilia (80 percent of cases)[2]	D66
Hemophilia B	Caused by a decreased or absent levels of **clotting factor IX** (20 percent of cases)[2]	D67
Von Willebrand Disease	The result of missing or defective von Willebrand Factor (VWF), which is a clotting protein necessary to prevent bleeding.[3]	D68.0

Mild vs. Severe: Along with the different types of hemophilia, patients may have varying severity based on their clotting factor levels. Mild hemophilia may result in abnormal bruising and bleeding, but not to an extent where chronic treatment is necessary. Severe hemophilia requires chronic treatment due to increased bleeding episodes, especially inside the body.[2]

Who Is Affected?

- About **1 in 4,000 to 5,000** babies born in the United States are diagnosed with hemophilia A[4]
- **Males are more commonly affected** than females[5]
- The **median age of diagnosis is 36 months** (can be as early as one month with severe cases)[4]
- With about **two-thirds of cases**, there is a **family history** of hemophilia[4]
- Females can be carriers of the genes; however, most (about 90 percent) will be asymptomatic[5]
- **Presentation is equal among all races and ethnic groups**[5]

Treatment Options

Current treatment regimens for hemophilia are based on severity and can include:

- **Recombinant Factor Concentrates** – Currently the most common type of treatment[6]
  - Those with more severe cases receive these treatments on a scheduled basis to prevent bleeds
  - Those with mild cases may receive clotting factor replacement on an as needed basis if at risk for active bleeds
- **Desmopressin** may be used for mild cases to stimulate the release of stored factor VIII[6]
- **Antifibrinolytics Agents** (such as Amicar® and Cyklokapron®) are used for nasal and oral bleeds; they also may be used prior to dental appointments[6]
- **Plasma Clotting Factor Concentrates** may also be given to help replenish clotting factors throughout the body[6]

With current Recombinant Factor products, it is possible for patients to develop **inhibitors**. Inhibitors prevent the current factor treatments from working the same as before, therefore, making it more difficult to prevent or stop a bleeding episode.[6] The presence of inhibitors requires the use of increased doses, and can end up costing greater than $1 million per year, versus $400,000 – $900,000 for severe patients without inhibitors.*

New Treatment: Gene Therapy

A new gene therapy, **Roctavian™** (valoctocogene roxaparvovec) casually known as "val-rox," is expected to receive its FDA-approval decision by the end of August 2020. Roctavian™ is a single infusion therapy used to treat hemophilia A in those who are over 18 years of age, who are without the presence of inhibitors and who do not have a previous diagnosis of liver disease.[7] This will be the first gene therapy to be approved for the treatment of hemophilia. The FDA also accepted the pre-market approval application for an AAV5 (adeno-associated virus) antibody assay, which would be used as a combination diagnostic tool. It is estimated that about 80 percent of patients with hemophilia A do not have immunity to AAV5. Those with active AAV5 immunity could be ineligible for this gene therapy's use.[8]

Continued...

New Treatment: Gene Therapy, *continued*

To date, 15 patients have received the gene therapy as part of a clinical trial. The median factor levels present still met the criteria to define hemophilia. None of the patients restarted chronic factor treatment after the first three years, and bleeding episodes reportedly decreased significantly.[9]

Treatment Details

	Standard Half-Life Recombinant Factor VII Products (Recombinate®, Kogenate®, Advate®)	Extended Half-Life Recombinant Factor VII Products (Elocate®, Adynovate®, Jivi®, Esperoct®)	Hemlibra®	Roctavian™
FDA Approved Use	The treatment of hemophilia A **without** inhibitors	The treatment of hemophilia A **without** inhibitors	The treatment of hemophilia A **with or without** inhibitors	The treatment of hemophilia A **without** inhibitors
Population	As many as 2,700 females[10] and 33,000 males are currently living with hemophilia. About 400 babies are born with hemophilia each year.[4] 8,200 patients have severe hemophilia A, with 2,000 of those not having inhibitors.[11]			
FDA Approved Dosing	Intravenous infusion based on weight and desired factor increase	Intravenous infusion based on weight and desired factor increase	Subcutaneous weight based injection every 1, 2 or 4 weeks based on individualized regimen	One time intravenous infusion
Average Annual Cost for Chronic prophylaxis in Adults*	$800,000	$800,000	$800,000	More than $2 million
Payment Structures	Medical and/or Prescription Benefits	Medical and/or Prescription Benefits	Medical and/or Prescription Benefits	Medical
HCPCS Codes for Medical Billing	J7192	J7205, J7207, J7208, J7199	J7170	Unavailable

**All costs estimated using AMS PredictRx and the standard weight of 72kg.*

On the Horizon

The hemophilia gene therapy market is very competitive with additional manufacturers such as uniQure, Sangamo Therapeutics and Intellia Therapeutics having their own gene therapies for hemophilia A and B in late phase studies.

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**.

References: [1]"Hemophilia," Mayo Clinic, https://www.mayoclinic.org/diseases-conditions/hemophilia/symptoms-causes/syc-20373327, accessed June 3, 2020; [2]"Hemophilia, Patient Education," Clinical Pharmacology, https://www-clinicalkey-com.authenticate.library.duq.edu/pharmacology/education/disease-information?di=102574, accessed June 3, 2020; [3]"Von Willebrand Disease," National Hemophilia Foundation, https://www.hemophilia.org/Bleeding-Disorders/Types-of-Bleeding-Disorders/Von-Willebrand-Disease, accessed June 3, 2020; [4]"Data & Statistics on Hemophilia," CDC, https://www.cdc.gov/ncbddd/hemophilia/data.html, accessed June 3, 2020; [5]"Hemophilia A," NIH-GARD, https://www.rarediseases.info.nih.gov/diseases/6591/hemophilia-a, accessed June 3, 2020; [6]"Treatment of Hemophilia," CDC, https://www.cdc.gov/ncbddd/hemophilia/data.html, accessed June 3, 2020; [7]"Biomarin's Valrox, Possible 1st Gene Therapy for Hemophilia A, Under FDA Priority Review," Hemophilia News Today, https://hemophilianewstoday.com/2020/02/24/biomarins-valrox-possible-first-gene-therapy-hemophila-a-under-fda-priority-review-marketing-application-accepted/, accessed June 3, 2020; [8]"Valoctocogene Roxaparvovec (BMN 270) for Hemophilia A," BIOMARIN, https://www.biomarin.com/products/pipeline/bmn-270/, accessed June 3, 2020; [9]"Multiyear Follow-up of AAV5-hFVIII-SQ Gene Therapy for Hemophilia A," New England Journal of Medicine, https://www.nejm.org/doi/full/10.1056/NEJMoa1908490, accessed June 10, 2020; [10]"Women Can Have Hemophilia, Too," CDC, https://www.cdc.gov/ncbddd/hemophilia/features/women-and-hemophilia.html, accessed June 5, 2020; [11]"American Thrombosis and Hemostasis Network," ICER, https://www.icer-review.org, Accessed June 5, 2020.

Products are underwritten by HM Life Insurance Company, Pittsburgh, PA, Highmark Casualty Insurance Company, Pittsburgh, PA, or HM Life Insurance Company of New York, New York, NY.

This is an informational document only and is not intended to provide legal advice, tax advice or advice on your health plan's content and design. This document is not meant to address federal or other applicable laws for health plans. This document only includes HM's suggested best practices for certain provisions in a health plan. You should consult with your legal counsel and/or a qualified plan design professional.

HM INSURANCE GROUP
Guarding Financial Health
800.328.5433 | hmig.com

MTG-3295 (6/20)