HEMOPHILIA
Background, new developments, key strategies

INTRODUCTION

Hemophilia is a rare, inherited bleeding disorder in which the blood does not clot properly.
- **20,000** patients in the US
- Occurs in **1 of 5,000** male births
- Affects **MALES** almost exclusively
- Extremely rare, but extremely **expensive**: Ranks **8th most costly** for employers for all specialty diseases

Hemophilia is caused by a mutation that disrupts the body’s ability to produce clotting factor proteins. There are two main forms of the disease, labeled A and B.

Low levels of clotting factor can lead to spontaneous bleeding in the joints or internal organs, or even inside the skull. Uncontrolled bleeding can cause joint disease, seizures and paralysis or death.

Hemophilia can be mild, moderate, or severe. The lower the amount of the factor, the more likely it is that bleeding will occur.

MISSING LINK

Lack of clotting factor reduces the body’s ability to control bleeding.

### Injury Occurs

- Injury to blood vessel results in bleeding.
- Vessel constricts and clotting factors are activated.

**Normal**
- Natural clotting factor helps form a strong platelet plug.
- A stable fibrin mesh forms a sealed clot over the platelet plug to stop the bleeding.

**Hemophilia**
- Lack of natural clotting factor means only a weak platelet plug can form.
- Incomplete fibrin mesh allows bleeding to continue.

All but the mildest forms of hemophilia are extremely expensive to treat. Unfortunately, the majority of people with hemophilia have the most severe form.

Of all people with hemophilia...

- **25%** Mild: 6-30% of normal clotting factor; may not be diagnosed until after serious injury
- **15%** Moderate: 1-5% of normal clotting factor; some possible spontaneous bleeding, or after injury
- **60%** Severe: less than 1% of normal level of clotting factor; constant danger of bleeding episodes


Critical Breakthrough: Replacement Clotting Factor

Compact, effective forms of replacement clotting factor helps many hemophilia patients live near-normal lives.³

Hemophilia therapy consists of replacement therapy — artificially raising a patient’s level of clotting factor via infusion.³

Fresh plasma contains only trace amounts of clotting protein and huge amounts were needed to control bleeding. Researchers learned to make concentrated forms of factor, but these still required thousands of units of donated plasma to prepare just one unit of concentrate.³

Modern factor concentrates are made either with donated human blood plasma, or, beginning in the 1990’s, patients began using genetically engineered clotting factor.³

Both forms of clotting factor are easy to store, mix, and use at home, so many patients self-administer their factor. It only takes about 15 minutes to receive the factor.³

Immunity

Some patients develop immunity to their infusions

About 30% of type A and 5% of type B patients on preventive therapy develop immunity to the clotting factors called inhibitors.⁴ Inhibitors make treatment of bleeding episodes much more complicated, which drives up factor costs - up to or over $1 million per year is not uncommon.⁴

≥$1 million

Total annual cost
UNDERSTANDING TREATMENT COSTS

Hemophilia treatment costs can be extremely variable at the individual patient level. At the aggregate level, we can expect overall treatment spending to rise over time as hemophilia patients live longer and as new treatments come into play.

**Clotting factor costs**

One key cost variable is how much replacement clotting factor a patient needs. Mild and moderate cases require relatively little replacement factor, while severe cases need much more. Patients on preventive therapy use the most replacement factor but also show fewer bleeding episodes and ER visits.

![Graph showing clotting factor costs](image_url)

**Nearly all spending (94%) for severe cases is due to factor costs. Compare to just over half (54%) for mild cases.**

**Immunity (inhibitors) to factor infusions**

The chart below illustrates the explosive effect inhibitors have on costs when inhibitors and comorbidities are added.

**Health Care Costs for Hemophilia in Commercially Insured Populations**

![Cost chart](image_url)

Children with Type A: $142,057

Adults with Type A plus HIV/HCV: $188,056

All males with Type A: $144,306

Without inhibitors: $696,279

Including inhibitors: $831,866

Without inhibitors: $577,640

Without inhibitors: $188,056
PREDICTING FUTURE TREATMENT SPENDING

While factor concentrate is expensive, purchase prices have remained fairly flat and are expected to remain so in the short term. Therefore, predicting costs over the short term means understanding the age profile of each patient. Over the longer term, overall treatment costs will go up due to demographic pressures.

Long Term

Costs will rise as growing numbers of patients live longer and develop additional complications (e.g., obesity, low bone density).

Better treatments have increased Hemophiliac life expectancy

![Graph showing life expectancy for hemophiliacs from 1900 to today](image)


Short Term

Hemophilia patients experience radical changes in the cost of their disease as they age.

Payer costs change significantly by patient age

![Graph showing annual health insurance expenditure per patient](image)

PROMISING TECHNOLOGY

Some of the highest costs for hemophilia are due to patients who develop inhibitors (resistance) to the factor itself. Unfortunately, treatments to overcome resistance are expensive (~$1 million) and not always effective. This promising research aims to prevent the immune system from producing inhibitors.

Preventing Inhibitor resistance

Genetically engineered plant cells can be coaxed to produce type A and B factor proteins as part of their normal cell machinery. While plant proteins cannot be used to directly promote clotting, they can help “desensitize” the body’s immune system and prevent rejection.

Note: Although human figures are used below, these studies are still in the animal phase. Human trials are expected to begin sometime in 2015.

1. Lettuce leaf chloroplasts are genetically engineered to produce human clotting factor protein.
   
   About 10,000 chloroplasts are in each cell.

2. The resulting plant-based factor cannot be used directly to control bleeding.
   Instead, the engineered lettuce and clotting protein is freeze dried, powdered and administered by adding to food.

3. The leaf cells protect clotting proteins from stomach acids.
   Cells release proteins once inside the intestinal tract.
   Another protein is added to help clotting factor bind to the intestinal wall.
   Clotting proteins are then processed by the immune system to produce tolerance.

4. The plant-based clotting protein “defuses” the immune system.
   Real clotting factor infusion can proceed with no allergic reaction.
   Any existing inhibitors are reversed.

OVERVIEW OF HEMOPHILIA MANAGEMENT PROGRAM
Integrated management from BriovaRx® specialty pharmacy ensures consistent management and holistic care coordination.

**BriovaRx Program Goals**

- **Clinical Management**
  Provides individualized educational and clinical support for patients to help improve adherence to achieve optimal outcomes.

- **Utilization Management**
  Ensure clinically appropriate and cost-effective utilization by using the management strategies available to each client.

- **Aggressive contracting**
  Leading to better drug pricing.

- **Available Networks**
  Access to efficient, quality care and deep discounts for many specialty drugs.

- **Assay Management**
  We tightly manage how much factor medication is dispensed reduces waste and can save thousands of dollars per patient per year.

**DEDICATED CALL CENTER**

We have a dedicated call center for hemophilia. The same specialty pharmacist within BriovaRx specialty pharmacy will regularly assess each patient’s needs.

- Ongoing support to recognize and prevent bleeds
- Comprehensive assessments 2-4X per year
- Teach patients and caregivers how to "self-infuse" at home
- Ensure ready access to clotting factor
- Conduct routine compliance and adherence calls
- Supplies needed such as needles, tubing, syringes, etc.

**SPECIALTY PHARMACY HEMOPHILIA PROGRAM**

The BriovaRx specialty pharmacy hemophilia program is designed to make patients as self-sufficient as possible. We also work closely with regional Hemophilia Treatment Centers (HTCs), that bring together specialty teams of doctors, nurses, & health professionals.

The BriovaRx specialty pharmacy connects patients with the nearest local HTC which monitors each patient’s treatment.

**HTCS ARE LOCATED ACROSS THE COUNTRY**

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MEMBERS
Better health and support and guidance

CLIENTS
Total cost control and program management: clients can achieve up to $0.66 PMPM savings by exclusively using participating providers*

PROVIDERS
Better health support and guidance

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*Exclusive use of participating providers can result in significant savings for members. Savings and results may vary.
Hemophilia Insight Report

MEET JOHN

John was diagnosed with severe hemophilia when he was an infant. Without effective preventive therapy he would risk spontaneous bleeding, disability or death. John was transitioned into the BriovaRx hemophilia specialty pharmacy program shortly after his employer switched to OptumRx.

What does it mean to manage the total cost of John’s condition?

Synchronize member touch points and data into ONE system.

<table>
<thead>
<tr>
<th>Opportunities</th>
<th>Traditional PBM</th>
<th>OPTIMIZED*</th>
<th>OptumRx Connected Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Prior Authorization</td>
<td>YES</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>2 Assay Management</td>
<td>NOT OPTIMIZED</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>3 Adherence Programs</td>
<td>NOT OPTIMIZED</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>4 Clinical Management Program</td>
<td>NOT OPTIMIZED</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>5 Connect members with quality physicians and Hemophilia Treatment Centers</td>
<td>MISSED</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>6 Manage co-morbid depression with synchronized behavioral referrals</td>
<td>MISSED</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>7 Weight monitoring and healthy lifestyle programs to encourage condition-appropriate exercises and diet</td>
<td>MISSED</td>
<td>✓</td>
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</tr>
</tbody>
</table>

A traditional PBM looking only at pharmacy claims or pharmacy solutions can miss opportunities. Our ONE team approach manages multiple consumer touch points to promote real behavior change, like lower cost alternatives, medication adherence or engagement in clinical management programs.

Our Connected Care model leverages all member touch points to capitalize on every opportunity to guide each member to their best next health action.

* The synchronized care management model described here depends on a minimum specific set of OptumHealth care management services, plus OptumRx pharmacy services. Please speak to your OptumRx or UnitedHealthcare representative for more information about how synchronization can work for you.

Connected Engagement:
Every interaction is an opportunity to reduce health risk and lower costs

Synchronized Touch Points

Self Service + Outreach + Inbound

Optum  www.optum.com
THE OPTUMRx DIFFERENCE: HEALTH CARE CONNECTED

Even ordinary PBMs can do an adequate job at the ordinary things PBMs do – negotiate discounts, pay claims, manage formularies and so on. But OptumRx is more than an ordinary PBM: We are a complete pharmacy care services company. We focus on managing total condition spending by connecting pharmacy’s impact across all benefits.

*Estimated additional savings over traditional core PBM services based on total pharmacy spend. Illustrative only; results may vary.
References


For more information about how you can manage the cost of Hemophilia, please contact your OptumRx representative.