What You Need to Know: Blood Factors for Hemophilia

Mandy C. Leonard, Pharm.D., BCPS
System Director, Drug Use Policy and Formulary Management
Cleveland Clinic
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The speaker has no actual or potential conflict of interest in relation to this presentation
Objectives

• Review different types of hemophilia
• Describe blood factors used in the management of hemophilia
• List formulary considerations for blood factors for hemophilia
• Review procurement, billing, and financial impact of blood factors for hemophilia
Definitions

- Hemophilia - inherited bleeding disorders
  - Hemophilia A
  - X-linked recessive disorder (factor VIII)
  - Hemophilia B (factor IX)
  - X-linked recessive disorder
  - von Willebrand disease (VWD)
  - Inherited abnormality in von Willebrand factor (VWF)
  - Acquired factor deficiencies (inhibitors)
Clotting Cascade

Contact activation (intrinsic) pathway

Tissue factor (extrinsic) pathway

Prothrombin (II)

Fibrinogen (I)

Cross-linked fibrin clot

Common pathway

Blood Factors for Hemophilia
Hemophilia A

- Defective synthesis of factor VIII
  - Mutation on long-arm of X chromosome
  - Absent or reduced circulating levels of factor VIII
  - Ultimately leading to decreased thrombin generation

- Discovered as early as 2\textsuperscript{nd} century and in the 19\textsuperscript{th} century
  sex-linked inheritance patterns documented

- Incidence 1 in every 5,000 to 7,000 live male births
  - Severe hemophilia usually diagnosed in first 1 to 1.5 years of life

- Hemophilia A in females is extremely rare
All daughters of a hemophilic male are carriers of hemophilia, whereas all sons are normal

<table>
<thead>
<tr>
<th>Normal Female XX</th>
<th>Hemophilic Male X^hY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(XX^h) (Carrier Female)</td>
</tr>
<tr>
<td></td>
<td>(XX^h) (Carrier Female)</td>
</tr>
<tr>
<td>Carrier Female</td>
<td>Normal Male</td>
</tr>
<tr>
<td>----------------</td>
<td>-------------</td>
</tr>
<tr>
<td>$X^hX$</td>
<td>$XX^h$</td>
</tr>
<tr>
<td></td>
<td>(Carrier Female)</td>
</tr>
<tr>
<td></td>
<td>$XX$</td>
</tr>
<tr>
<td></td>
<td>(Normal Female)</td>
</tr>
</tbody>
</table>

Daughters of carriers have a 50% chance of being a carrier, whereas sons of carriers have a 50% chance of having hemophilia; prenatal screening.

Note: In many cases, there is no family history of hemophilia; at least 30% of cases are due to spontaneous (de novo) mutations.

Clinical Features of Hemophilia A

- Excessive bleeding into various tissues of the body, including soft tissue hematomas and bleeding in joint spaces *(recurrent hemarthroses; 75% of bleeding episodes)*

<table>
<thead>
<tr>
<th>Classification</th>
<th>Factor VIII Level</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>6-40% of normal (0.06-0.40 U/ml)</td>
<td>Hemorrhage secondary to trauma/surgery&lt;br&gt;Rare spontaneous hemorrhage</td>
</tr>
<tr>
<td>Moderate</td>
<td>1-5% of normal (0.01-0.05 U/ml)</td>
<td>Hemorrhage secondary to trauma/surgery&lt;br&gt;Occasional spontaneous hemorrhage</td>
</tr>
<tr>
<td>Severe</td>
<td>≤1% of normal (≤ 0.01 U/ml)</td>
<td>Spontaneous hemorrhage from early infancy&lt;br&gt;Frequent spontaneous hemarthroses; other hemorrhages; factor replacement</td>
</tr>
</tbody>
</table>

Hemarthroses - Knee
Laboratory Features of Hemophilia A

- Prolonged activated partial thromboplastin time (aPTT)
  - aPTT corrects when hemophilic plasma is mixed with an equal volume of normal plasma

- Normal prothrombin time (PT) and thrombin clotting time

- Factor VIII activity
  - One-stage clotting assay based on aPTT

- Differentiated from VWD
  - Carrier of factor VIII
  - Half-life of factor VIII shortened
Management of Hemophilia A

• Avoid aspirin, NSAIDs, and other medications that interfere with platelet aggregation; intramuscular injections

• Mild-to-moderate: desmopressin (DDAVP)
  – 0.3 mcg/kg IV/SC (factor VIII levels increase 2- to 3-fold)
  – 150 to 300 mcg intranasal spray
  – Tachyphylaxis

• Fresh-frozen plasma; cryoprecipitate

• Factor VIII replacement therapy (intravenous)
  – Prophylaxis
    – Home therapy
  – Treatment

### Blood Factors for Hemophilia A - Inherited Human *Plasma-Derived* Factor VIII Concentrates

<table>
<thead>
<tr>
<th>Name</th>
<th>Manufacturer</th>
<th>Origin</th>
<th>Viral Inactivation</th>
<th>Suggested Wholesale Price (SWP) per unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemofil M</td>
<td>Baxter/Baxalta</td>
<td>Plasma</td>
<td>Solvent-detergent</td>
<td>$1.60</td>
</tr>
<tr>
<td>Monoclate-P</td>
<td>CSL Behring</td>
<td>Plasma</td>
<td>Pasteurization</td>
<td>$1.30</td>
</tr>
</tbody>
</table>

- These are designated as ultrapure products
- Monoclonal antibody affinity-purified plasma-derived factor concentrates
- Improved viral-depleting process and donor screening practices have reduced risk for transmission of HIV and hepatitis B and C; however, recombinant products are recommended.

[www.hemophilia.org](http://www.hemophilia.org) [Accessed March 21, 2016]
## Blood Factors for Hemophilia A- Inherited

**Recombinant Factor VIII Concentrates**

<table>
<thead>
<tr>
<th>Name</th>
<th>Manufacturer</th>
<th>Origin</th>
<th>Viral Inactivation</th>
<th>SWP per unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advate</td>
<td>Baxter/Baxalta</td>
<td>3rd generation; CHO</td>
<td>Solvent-detergent</td>
<td>$1.82</td>
</tr>
<tr>
<td>Helixate FS</td>
<td>Bayer (CSL Behring)</td>
<td>BHK</td>
<td>Solvent-detergent</td>
<td>$1.76</td>
</tr>
<tr>
<td>Kogenate FS</td>
<td>Bayer</td>
<td>2nd generation; BHK</td>
<td>Solvent-detergent</td>
<td>$1.75</td>
</tr>
<tr>
<td>Recombinate</td>
<td>Baxter/Baxalta</td>
<td>1st generation (albumin); CHO</td>
<td>Solvent-detergent</td>
<td>$1.82</td>
</tr>
<tr>
<td>Xyntha</td>
<td>Pfizer</td>
<td>3rd generation; CHO</td>
<td>Solvent-detergent</td>
<td>$1.82</td>
</tr>
<tr>
<td>Kovaltry</td>
<td>Bayer</td>
<td>3rd generation; BHK</td>
<td>Solvent-detergent; nanometer filtration</td>
<td>$2.04</td>
</tr>
<tr>
<td>Eloctate</td>
<td>Biogen</td>
<td>EHK</td>
<td>Prolonged half-life</td>
<td>$2.38</td>
</tr>
</tbody>
</table>

CHO=Chinese hamster ovarian cells; BHK= baby hamster kidney cells; EHK=human embryonic kidney cells

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[www.hemophilia.org](http://www.hemophilia.org) [Accessed March 21, 2016]

ASD Healthcare
Dose of Factor VIII Replacement Therapy

- 1 unit factor VIII per ml of plasma = 100% normal
  - 1 unit factor VIII/kg raises circulating factor VIII level by ~0.02 unit/ml or 2 units/dL

- Desired level of factor VIII
  - Prophylaxis versus treatment

- Dose required to raise level dependent on patient’s plasma volume
  - 5% body weight (kg)
  - Plasma volume 70 kg patient = 3500 ml
  - Dose of FVIII (IU) = Weight (kg) x (desired % increase) x 0.5

- Achieve normal factor VIII levels of 1 unit/ml (100%) =
  - Loading dose (for 70 kg patient): 3500 factor VIII units
  - Half-life = 8 to 12 hours
  - Maintenance dose: 1750 units every 12 hours
**Examples of Doses of Factor VIII Replacement Therapy for Treatment of Hemorrhage**

<table>
<thead>
<tr>
<th>Site</th>
<th>Desired Factor VIII Level (% of normal)</th>
<th>Factor VIII (Unit/kg BW)</th>
<th>Frequency (hours) Adjusted per patient</th>
<th>Duration (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemarthroses</td>
<td>30-50</td>
<td>25</td>
<td>12-24</td>
<td>1-2</td>
</tr>
<tr>
<td>GI tract</td>
<td>50-100</td>
<td>50</td>
<td>12</td>
<td>7-10</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>30-50</td>
<td>25</td>
<td>12</td>
<td>Until resolved</td>
</tr>
<tr>
<td>Hematuria</td>
<td>30-100</td>
<td>25-50</td>
<td>12</td>
<td>Until resolved</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>50-100</td>
<td>50</td>
<td>12</td>
<td>7-10</td>
</tr>
</tbody>
</table>

Note: May be administered as bolus injections or as continuous infusions (150 to 300 units per hour)

**Patient Case**

- Patient with hemophilia A presents with epistaxis
- Increase factor VIII level by 30%
  - From 0 to 30%, or 10 to 40%
- Patient weighs 50 kg
- Recommended dose of factor VIII replacement therapy is 750 IU
  - $50 \text{ kg} \times 30 \text{ (desired \% increase)} \times 0.5$
- Administered every 12 hours (adjust as needed)
Replacement of Factor VIII for Surgical Procedures

- Emergent versus elective surgery
- Factor VIII raised to normal levels before surgery and maintained for 7 to 10 days or until healing complete
- Continuous infusion, or bolus injections (every 8-12 hours)
- Factor VIII levels monitored
- Bone/joint surgery- prolonged factor VIII replacement
Hemophilia A (Inherited) and Inhibitors to Factors VIII

• Main complication of factor VIII replacement therapy is development of specific inhibitor antibodies that neutralize factor VIII

• Prevalence: 3 to 26%

• High-risk:
  – Genetic mutations (family history of inhibitors)
  – Ethnicity (African Americans>Hispans>Caucasians)
  – Severe hemophiliacs treated at an early age

• aPTT of a 1:1 mixture of plasma with inhibitor and normal plasma is significantly prolonged after incubations at 37°C for 1 to 2 hours
  – Bethesda assay/Nijmegen assay

Lollar P. J Thromb Haemost. 2004;2;1082.
## Hemophilia A (Inherited) and Inhibitors to Factors VIII

<table>
<thead>
<tr>
<th>Type of Responder</th>
<th>Initial Titer</th>
<th>Minor Hemorrhage</th>
<th>Major Hemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>&lt;5 BU</td>
<td>Factor VIIa; FEIBA</td>
<td>Factor VIII; Factor VIIa, FEIBA</td>
</tr>
<tr>
<td>High</td>
<td>&gt;5 BU</td>
<td>Factor VIIa; FEIBA</td>
<td>Factor VIIa; FEIBA</td>
</tr>
<tr>
<td>Low</td>
<td>&lt;5 BU</td>
<td>Factor VIIa; FEIBA</td>
<td>High-dose Factor VIII (10,000 to 15,000 units, then 1000 units/hour)</td>
</tr>
</tbody>
</table>

**BU** = Bethesda units

Clotting Cascade

Contact activation (intrinsic) pathway

Tissue factor (extrinsic) pathway

Trauma

TFPI

VIIa

VII

VIII

VIIIa

IXa

VIIa

VII

Antithrombin

Prothrombin (II)

Fibrinogen

Fibrin

XII

XIa

IX

V

Va

Xa

Thrombin (IIa)

Common pathway

Cross-linked fibrin clot

XIIIa

XIII

Blood Factors for Hemophilia
Hemophilia A (Inherited) and Inhibitors to Factors VIII

- **FEIBA (Baxter/Baxalta)- human plasma-derived prothrombin complex concentrate (PCC)**
  - Contains factors II, VIIa, IX, and X
  - Able to bypass an inhibitor to factor VIII or IX
  - 50 to 100 units/kg every 8 to 12 hours (patient dependent)
  - SWP: $2.59 per unit

- **NovoSeven RT (Novo Nordisk)- recombinant factor VIIa concentrate**
  - Contains *activated* factor VIIa
  - Activates factor X
  - Associates with factor Va and converts prothrombin to thrombin
  - 90 to 120 mcg/kg every 2 to 3 hours
  - SWP: $2.40 per mcg
Hemophilia A- Acquired

• Rare autoimmune disease, not inherited
  – Approximately 500 cases per year in United States
  – Median age for diagnosis: 74 years
  – Delayed diagnosis

• Immunoglobulin G (IgG) antibodies bind to domains on factor VIII (neutralizes function)

• Manifests as spontaneous bleeding and can be life-threatening
  – Skin, muscles (45%), soft tissue, and mucous membranes, gastrointestinal/intra-abdominal bleeds (23%)

• Unlike hemophilia A (mixing test), if patient has autoantibody inhibitor to factor VIII, then the factor VIII in normal plasma will also be inhibited and the aPTT will not normalize

# Blood Factors for Hemophilia A- Acquired

<table>
<thead>
<tr>
<th>Name</th>
<th>Manufacturer</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>NovoSeven RT</td>
<td>NovoNordisk</td>
<td>Also used in hemophilia A inherited with inhibitors</td>
</tr>
<tr>
<td>FEIBA</td>
<td>Baxter/Baxalta</td>
<td>Also used in hemophilia A inherited with inhibitors</td>
</tr>
<tr>
<td>Obizur (recombinant porcine factor VIII)</td>
<td>Baxter/Baxalta</td>
<td>Hemophilia A- acquired only; Human factor VIII inhibitors do not cross react with porcine factor VIII</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Initial dose: 200 units/kg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adjusted dose per factor VIII level (50-100 units/kg) and administer every 4 to 12 hours</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SWP per unit: $6.19</td>
</tr>
</tbody>
</table>

Obizur [prescribing information]. Westlake Village, CA: Baxter Healthcare Corporation; October 2014. ASD Healthcare
Hemophilia B

• Defective synthesis of factor IX
  – Mutation on long-arm of X chromosome
  – Absent or reduced circulating levels of factor IX
  – Ultimately leading to decreased thrombin generation

• Christmas disease
  – Named for first patient diagnosed in 1952

• Incidence 1 in every 25,000 to 30,000 live male births

• Genetic inheritance is similar to hemophilia A
  – Carriers are typically asymptomatic
  – Prenatal screening

Clinical Features of Hemophilia B

• *Clinically indistinguishable* from Hemophilia A
• Fewer and less severe complications
• Hemarthroses

<table>
<thead>
<tr>
<th>Classification</th>
<th>Factor IX Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>5 to 40% of normal</td>
</tr>
<tr>
<td>Moderate</td>
<td>1 to 5% of normal</td>
</tr>
<tr>
<td>Severe</td>
<td>&lt;1% of normal</td>
</tr>
</tbody>
</table>

Factor IX inhibitors are much less common; only ~3% of severe patients develop inhibitors
Laboratory Features of Hemophilia B

• Similar to hemophilia A
• Prolonged activated partial thromboplastin time (aPTT)
  – aPTT corrects when hemophilic plasma is mixed with an equal volume of normal plasma
• Normal prothrombin time (PT)
• Factor IX activity
  – One-stage clotting assay based on aPTT
• Must be distinguished from hemophilia A

Management of Hemophilia B

- Similar to Hemophilia A
  - Avoid select medications; intramuscular injections
- Factor IX replacement therapy
## Blood Factors for Hemophilia B
Human *Plasma-Derived Factor IX Concentrate*

<table>
<thead>
<tr>
<th>Name</th>
<th>Manufacturer</th>
<th>Classification</th>
<th>Viral Inactivation</th>
<th>SWP per unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>AlphaNine SD</td>
<td>Grifols</td>
<td>High-purity</td>
<td>Solvent-detergent; virus filtered</td>
<td>$1.58</td>
</tr>
<tr>
<td>Mononine</td>
<td>CSL Behring</td>
<td>High-purity</td>
<td>Ultrafiltration; chemical</td>
<td>$1.52</td>
</tr>
</tbody>
</table>

Improved viral-depleting process and donor screening practices have reduced risk for transmission of HIV and hepatitis B and C; however, recombinant products are recommended.
Blood Factors for Hemophilia B
*Recombinant* Factor IX Concentrate

<table>
<thead>
<tr>
<th>Name</th>
<th>Manufacturer</th>
<th>Origin</th>
<th>Viral Inactivation</th>
<th>SWP per unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>BeneFIX</td>
<td>Pfizer</td>
<td>CHO</td>
<td>Solvent-detergent</td>
<td>$1.64</td>
</tr>
<tr>
<td>Ixinity</td>
<td>Emergent Biosolutions</td>
<td>CHO</td>
<td>Solvent-detergent; nanofiltration</td>
<td>$1.78</td>
</tr>
<tr>
<td>Rixubis</td>
<td>Baxter/Baxalta</td>
<td>CHO</td>
<td>Nanofiltration</td>
<td>$1.75</td>
</tr>
<tr>
<td>Alprolix</td>
<td>Biogen</td>
<td>EHK</td>
<td>Chromatography; Prolonged half life</td>
<td>$3.42</td>
</tr>
</tbody>
</table>

CHO=Chinese hamster ovarian cells; EHK=human embryonic kidney cells

www.hemophilia.org [Accessed March 21, 2016]
ASD Healthcare
Dose of Factor IX Replacement Therapy

• Desired level of factor IX

• Achieve 100% of normal = Dose 100 factor IX units/kg as bolus, then 50 factor IX units/kg every 12 to 18 hours
  – 60 kg patient = 6000 units (100%), then 3000 units
  – 250 units per hour as continuous infusion

• Monitor factor IX levels

• 1 unit factor IX/kg raises circulating factor IX level by 1% of normal or ~0.01 unit/ml

• Dose of factor IX (IU) = weight (kg) x (desired % increase) x F
  – F = reciprocal of observed recovery

Replacement of Factor IX for Surgery

• Emergent versus elective surgery
  – Desired factor IX level (%)
    – Minor (20-30%); Moderate (25-50%); Major (50-100%)
• Factor IX raised to normal levels before surgery and maintained for 7 to 10 days or until healing complete
• Continuous infusion, or bolus injections (every 12 to 24 hours)
• Factor IX levels monitored
• Bone/joint surgery- prolonged factor IX replacement

Hemophilia B and Inhibitors to Factor IX

• ~3% percent of severe hemophilia B
• <5 BU use large doses of factor IX replacement therapy
• >5 BU use same management as factor VIII inhibitor
  – Do not use Obizur
von Willebrand Disease

- von Willebrand factor (VWF) is a central component of hemostasis
  - Adhesive link between platelets and injured blood vessel wall
  - Carrier for factor VIII

- Most common inherited bleeding disorder

- Prevalence: 1 in every 1000

- Males and females

- Described by Eric von Willebrand in 1926
  - Bleeding disorder in 42/66 members of a family from Aland Islands (Finland)
  - Affected both males and females

## Classification of von Willebrand Disease

<table>
<thead>
<tr>
<th>Type</th>
<th>Frequency</th>
<th>Genetics</th>
<th>VWF levels</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1</td>
<td>1-30:1000</td>
<td>Autosomal dominant</td>
<td>Low (structure and function normal)</td>
<td>Most common variant</td>
</tr>
<tr>
<td>Type 2A</td>
<td>10-15%</td>
<td></td>
<td>Structure and function abnormal</td>
<td>Most common Type 2</td>
</tr>
<tr>
<td>Type 2B</td>
<td>&lt;5%</td>
<td></td>
<td></td>
<td>Thrombocytopenia</td>
</tr>
<tr>
<td>Type 2M</td>
<td>Rare (case reports)</td>
<td></td>
<td></td>
<td>Significant bleeding</td>
</tr>
<tr>
<td>Type 2N</td>
<td>Uncommon</td>
<td></td>
<td></td>
<td>Decreased binding</td>
</tr>
<tr>
<td>Type 3</td>
<td>1-5:1,000,000</td>
<td>Autosomal recessive</td>
<td>Low; undetectable</td>
<td>Most severe</td>
</tr>
</tbody>
</table>

Note: Types 1 and 3 are quantitative deficiencies and Type 2 is qualitative deficiency

Clinical Features of von Willebrand Disease

• Mucocutaneous bleeding (type 1)
  – Epistaxis (60%), bruising/hematomas (40%), menorrhagia (35%), gingival bleeding (35%), GI bleeding (10%)
  – After a trauma event (e.g., dental extraction, wound, post-partum, post-operatively)

• Hemarthroses (type 3)
Laboratory Features of von Willebrand Disease

• FVIII:C
  – Coagulant property of factor VIII protein (i.e., FVIII)

• VWF:Ag
  – Antigenic determinant(s) on factor VIII measured by immunoassays

• VWF:Rco
  – Property of VWF that supports ristocetin-induced agglutination of washed or fixed normal platelets
  – Most sensitive and specific single test for VWD

• VWF: <30 IU/dL (threshold)
Dose of VWD Factor Replacement Therapy

- Dosing and timing is largely empiric
- Goal to elevate the FVIII:C and VWF:RCo until bleeding stops and healing is complete
  - Initial replacement should be >100 IU/dL and maintenance >50 IU/dL for 7 to 14 days (major trauma/surgery) and 30 to 50 IU/dL (minor trauma/surgery) for 3 to 5 days; 50 IU/dL for 3 days (post-partum)
- VWF:RCo 50-100%
  - 20-40 IU/kg ristocetin cofactor activity raises plasma concentration by 50-100% or 0.7 units/ml
  - Loading Dose: 40-80 IU/kg
  - Maintenance dose is lower and administered every 8 to 12 hours

• Laboratory monitoring
Replacement of VWF for Surgery

• Hematologist/Surgeon
• Evaluate potential for bleeding
• DDAVP versus VWF replacement
Blood Factors for von Willebrand Disease
Factor VIII and von Willebrand Factor

<table>
<thead>
<tr>
<th>Name</th>
<th>Manufacturer</th>
<th>Use</th>
<th>SWP per unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alphanate</td>
<td>Grifols</td>
<td>Hemophilia A and vWD</td>
<td>$1.38</td>
</tr>
<tr>
<td>Humate-P</td>
<td>CSL Behring</td>
<td>Hemophilia A and vWD</td>
<td>$1.40</td>
</tr>
<tr>
<td>Wilate</td>
<td>Octapharma</td>
<td>vWD only</td>
<td>$1.56</td>
</tr>
</tbody>
</table>

Note: Patients with vWD type 1 and some patients with type 2 can be managed with desmopressin (~20-25% do not respond adequately to desmopressin)
Formulary Considerations: Blood Factors

• Hemophilia A
  – Recombinant product
  – Product for patient with inhibitors
  – Product for acquired hemophilia A

• Hemophilia B
  – Recombinant product
  – Product for patient with inhibitors

• VWD
  – VWF product
Blood Factors – Cost (Suggested Wholesale Price)

• Recombinate: $1.82 per IU
  – 1750 IU every 12 hours= $6,370 per day

• BeneFIX: $1.64 per IU
  – 2000 IU every 12 hours= $6,560 per day

• FEIBA: $2.59 per IU
  – 3500 IU every 12 hours= $18,130 per day

• NovoSeven RT: $2.40 per mcg
  – 6,300 mcg (6.3 mg) x 1 dose= $15,120
  – Every 2 to 3 hour dosing: ~$120,000

• Obizur: $6.19 per IU
  – Initial dose: $86,660, and $43,330 every 12 hours

• Humate-P: $1.40 per IU (VWF)
  – 3500 IU every 12 hours= $9,800 per day
Procurement of Blood Factors for Hemophilia

• Pharmacy versus Blood Bank

• Consignment versus on-demand ordering
  – Blood factor wholesaler

• Storage
  – Refrigerator space; some data for storage outside of refrigerator (dependent on product)

• Quantity sufficient to treat one hemophiliac patient urgently (emergent) for 48 to 72 hours
  – 20,000 units
  – Each lot varies per number of unit
  – Consult box/vial for exact potency

• Planned surgery/procedures
Blood Factor Stewardship

• Hematologists and pharmacists and nurses

• Process
  – Emergency versus elective admission
  – Notification of patient admission
  – Estimated total factor needed
  – Evaluate inventory (including units – dose rounding)
  – Order additional factor if needed

• Communicate
  – Prior to preparing and dispensing each dose
  – Extended stability

• Follow-up
Billing and Reimbursement for Blood Factors

• Pass-through status (inpatient)

• Document, document, document
  – Blood factor
  – Weight of patient (kg)
  – Dose
  – Frequency
  – Ordered, dispensed, administered via medication administration record

• Returns/Credits

• Patient Assistance Programs
Hemophilia Treatment Center (HTC)

• Specialized health care centers that bring together a team of doctors, nurses, and other health professionals experienced in treating people with hemophilia
  – Pathologists, Hematologists, Orthopedists, Physical Therapists, Genetic Counselors

• A CDC study of 3,000 people with hemophilia showed that those who used an HTC were 40% less likely to die of a hemophilia-related complication compared to those who did not receive care at a treatment center.

• Similarly, people who used a treatment center were 40% less likely to be hospitalized for bleeding complications

www.hemophilia.org [Accessed March 21, 2016]
Where are the HTCs located in Ohio?

• Children’s Hospital Medical Center of Akron
• Cincinnati Children’s Hospital Medical Center
• Dayton Children’s Hospital
• Nationwide Children’s Hospital (Columbus)
• Northwest Ohio Hemophilia Treatment Center (Promedica/Toledo Children’s Hospital)
• Ohio State University Medical Center (Columbus)
• University Hospital Health System (Cleveland)
• University of Cincinnati Medical Center
Summary

• There are different types of hemophilia, including hemophilia A and B as well as von Willebrand Disease

• Based on the type of hemophilia, there are specific management strategies including replacement of deficient or defective factor and replacement factors to bypass inhibitors

• There are several formulary considerations for blood factors for hemophilia including patient population, designation as a hemophilia treatment center, inventory/storage, and cost

• It is important to be prepared to manage hemophilia patients especially for emergent situations