Strengthening the Value of Managed Care and Specialty Pharmacy for Successful Management of Hemophilia

Satellite Symposium held in conjunction with AMCP Nexus 2016

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Medical Management Strategies to Integrate Hemophilia Care With Payer Policies

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Aetna
Learning Objective

• Describe current and evolving strategies for managed care organizations (MCOs) and specialty pharmacy providers to facilitate high-quality care for members with hemophilia
Hemophilia-Related Drug Costs Are Disproportionately Higher Than Disease Prevalence

Prevalence: 0.01%

0.001 PMPY Prescriptions

Average Cost Per Prescription: $7,519.16

PMPY=per member per year

Key Cost Variable Is Amount of Factor Replacement Needed

Nearly all spending for severe cases is due to factor costs compared to just over half for mild cases.
Prophylaxis and Inhibitors Contribute Significantly to Annualized Factor Costs

**Factor Costs in Hemophilia A***

<table>
<thead>
<tr>
<th>Category</th>
<th>Cost</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>$42,167</td>
<td>74</td>
</tr>
<tr>
<td>Moderate</td>
<td>$62,780</td>
<td>35</td>
</tr>
<tr>
<td>Severe Episodic</td>
<td>$159,761</td>
<td>67</td>
</tr>
<tr>
<td>Severe Prophylaxis</td>
<td>$275,324</td>
<td>123</td>
</tr>
<tr>
<td>Inhibitor</td>
<td>$721,603</td>
<td>16</td>
</tr>
</tbody>
</table>

*Factor costs in hemophilia B are similar

Reference prices: Medicare Average Sales Price.
Data from Hemophilia Utilization Group Study (HUGS). 2011.
Prophylaxis Decreases Overall Healthcare Utilization

Annual Number of ER Visits

<table>
<thead>
<tr>
<th></th>
<th>Days per patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Episodic</td>
<td>7.8</td>
</tr>
<tr>
<td>Prophylaxis</td>
<td>3.9</td>
</tr>
</tbody>
</table>

Length of Hospital Stay

<table>
<thead>
<tr>
<th></th>
<th>Days per patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Episodic</td>
<td>7.8</td>
</tr>
<tr>
<td>Prophylaxis</td>
<td>3.9</td>
</tr>
</tbody>
</table>

P=0.05

Patients With Inhibitors Have Higher Total Cost of Care

Based on analysis of pharmacy claims in the MarketScan Database for factor VIII prescription or bypassing agent during 2001–2007.

Payer Management Interventions Seek to Improve Care Quality and Manage Disease Costs

- **Appropriate Access**: Ensure appropriate use by linking the patients to the right drug administered at the right site of care.
- **Benefit Design**: Optimize pharmacy spend through appropriate benefit architecture to encourage appropriate utilization.
- **Care Optimization**: Maximize impact of hemophilia drug utilization through specialty pharmacy care.
- **Enabling Technology**: Leverage technology to collect and analyze data to support decision making across the continuum of care.
- **Network Contracts**: Leverage network pricing or (when eligible) federally supported drug discounts (eg, 340B).

Management Principles: Appropriate Access

**Right Patient**
- Included in product label
- Described in treatment guidelines
- Supported by clinical trial evidence and/or clinical experience

**Right Drug**
- Labelled indication
- Included in treatment guidelines
- Effective, safe, well tolerated
- Branded vs generic/biosimilar

**Right Quantity**
- Proper vial size (single vs multiple dose)
- Appropriate dose (assay management)
- Limit wastage
- Avoid “dosage creep”

**Right Site of Care**
- Inpatient
- Clinic
- Home health care
- Home; self-administered
Site of Care Can Have a Direct Impact on Cost

- At home; mobile infusion provider: $ to $$
- Physician’s office: $$$
- Freestanding infusion center/clinic: $$ to $$$
- Hospital outpatient department: $$$$
Management Principles: Benefit Design and Appropriate Utilization

- Member incentives for preferred drugs
- Use of cost tiers
- Incentives for
  - Preferred providers
  - Site of care
- Pharmacy and medical benefit integration

- Formulary management
- Preferred product
- Prior authorization
- Quantity limits
- Specialty distribution and management
- Minimize
  - Wastage
  - Inappropriate use

Balancing Cost and Care
Location of the Hemophilia Benefit: Medical or Pharmacy?

Challenges
- Member cost sharing often not coordinated across benefits
- Administration costs may not be measured
- Specialty rebates may not be paid to plan sponsor
- Little control over site of administration and distribution channels
- Different vendors for pharmacy vs medical benefit
- Medical data systems may not integrate into pharmacy systems

Allows health plan to utilize proven cost-containment tools

Harder for health plan to manage; no real-time adjudication
## Specialty Categories Under Pharmacy Benefit

<table>
<thead>
<tr>
<th>Rank</th>
<th>Therapy Class</th>
<th>PMPY Spend</th>
<th>Trend</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Utilization</td>
<td>Unit Cost</td>
</tr>
<tr>
<td>1</td>
<td>Inflammatory conditions</td>
<td>$89.10</td>
<td>10.3%</td>
<td>14.7%</td>
</tr>
<tr>
<td>2</td>
<td>Multiple sclerosis</td>
<td>$53.31</td>
<td>3.5%</td>
<td>6.2%</td>
</tr>
<tr>
<td>3</td>
<td>Oncology</td>
<td>$49.62</td>
<td>9.3%</td>
<td>14.4%</td>
</tr>
<tr>
<td>4</td>
<td>Hepatitis C</td>
<td>$38.44</td>
<td>-2.2%</td>
<td>9.2%</td>
</tr>
<tr>
<td>5</td>
<td>HIV</td>
<td>$31.53</td>
<td>4.6%</td>
<td>12.0%</td>
</tr>
<tr>
<td>6</td>
<td>Growth deficiency</td>
<td>$7.12</td>
<td>2.8%</td>
<td>2.8%</td>
</tr>
<tr>
<td>7</td>
<td>Cystic fibrosis</td>
<td>$6.64</td>
<td>12.5%</td>
<td>40.9%</td>
</tr>
<tr>
<td>8</td>
<td>Pulmonary hypertension</td>
<td>$5.85</td>
<td>13.4%</td>
<td>4.8%</td>
</tr>
<tr>
<td>9</td>
<td>Hemophilia</td>
<td>$5.79</td>
<td>4.9%</td>
<td>15.4%</td>
</tr>
<tr>
<td>10</td>
<td>Sleep disorders</td>
<td>$4.57</td>
<td>5.5%</td>
<td>18.5%</td>
</tr>
<tr>
<td><strong>TOTAL SPECIALTY</strong></td>
<td><strong>$341.21</strong></td>
<td><strong>6.8%</strong></td>
<td><strong>11.0%</strong></td>
<td><strong>17.8%</strong></td>
</tr>
</tbody>
</table>

PMPY = per member per year
Management Principles: Care Optimization

- Integrate hemophilia care into all network and medical management strategies
- Implement coordinated, multidisciplinary outpatient and home-based care
- Establish relationships with hemophilia treatment centers (HTCs), specialty pharmacy, and specialized medical providers
- Employ case management

Care Optimization

- Utilize treatment guidelines/clinical pathways
- Involve patients and caregivers in all decisions impacting their care
- Provide
  - Adherence programs
  - Patient/caregiver education
  - Behavior modification
  - Side effect management
  - Discharge management
Treatment Guidelines Provide Evidence-Based Recommendations for Delivery of Optimal Care

Ensure Delivery of Quality Care at the Best Price

• Utilize health care delivery strategies that may provide lower costs without sacrificing quality, including:
  • Centers of Excellence
  • Accountable Care Organizations (ACOs)
  • Patient-Centered Medical Homes (PCMHs)
• Comprehensive hemophilia treatment centers (HTCs) emphasize preventative services to reduce or eliminate complications
• Utilize networks of pharmacy providers, including specialty pharmacies, that can reduce drug costs through appropriate utilization
Integrated Comprehensive Hemophilia Care

- Patient
- Orthopedist
- Hematologist
- Nurse
- Physical Therapist
- Dentist
- Pharmacist
- Primary Care Physician
- Psychologist
- Social Worker
Collaboration Between Payers, Hemophilia Treatment Centers, and Specialty Pharmacy Providers Contributes to Optimizing Care
Management Principles: Enabling Technology

Enabling Technology

- Utilize technology to enhance collaboration between payers and providers
  - Analyze trends
  - Inform decision making
  - Track utilization and claims
  - Drive improvements in clinical and economic performance
- Incorporate technology to engage patients and encourage adherence
Innovative Tools and Resources Promote Patient Engagement and Adherence

**Live Multimedia**
- Live video education and counseling sessions with pharmacist

**Web-Based Tools and Mobile App**
- Easily accessible information to connect patients with education tools and community

**Written Patient Information Guide**
- Written resources to promote understanding of condition and treatment

**Community Resources**
- Educational and instructional videos designed to engage patients in disease management and treatment
Management Principles: Network Contracts

**Features**

- Integrated drug channel management strategies that ensure specialty drugs are dispensed through the most cost-effective and efficient pharmacy delivery channel
- 340B Drug Pricing Program provides outpatient drugs at a reduced price to safety-net providers

**Best Practices**

- Contract with experienced hemophilia pharmacy providers
- Ensure vendor manages factor cost through appropriate assay testing and product inventory management
- Develop policies to ensure correct dosing and stock for at-home use
- Monitor quality and accountability of pharmacy providers
Hemophilia Case Study

**Overview**
- Average cost per month for a hemophilia patient: $30,000
- Obtain necessary information from the ordering provider, including
  - Prophylaxis dose
  - Bleed dose
- Manage the specialty pharmacy

**Savings**
- Require specialty pharmacy to dispense within 5% of prescribed dose
  - Savings of up to $18,000 per patient
- Ensure only bleed doses are replaced when the member has a bleed
  - Accomplished through care management/PBM integration
  - Current industry practice is to fill all prophylaxis and bleed doses every month, without assessment of number of bleed doses on hand
  - Savings of up to $67,000 per patient
Alignment of All Stakeholders Ensures the Best Possible Patient Outcomes

- **Plan Sponsor – Provider**: Incentives based on quality decision-support technology
- **Provider**: More efficient use of services
- **Payer**: Focus on quality care outcomes
- **Plan Sponsor – Payer**: Plan design steerage to quality and efficiency

**HEMOPHILIA TREATMENT CENTER ACCESS**
While the traditional pharmaceutical trend has remained relatively flat, specialty drug spending has increased consistently over the past several years.

Hemophilia is a low-prevalence but high-cost disease, and patients require treatment across their lifespan with specialty therapeutics such as clotting factor concentrate and bypassing agents.

Access to care is necessary to optimize treatment outcomes; however, there is a need to strike a balance between cost and quality of care.

Several strategies have been devised to effectively manage cost and utilization while delivering high-quality care from the payer and specialty pharmacy perspective.
Managing Patients With Inhibitors: Coordinated Care for Optimal Outcomes

Steven Pipe, MD
Director, Division of Pediatric Hematology and Oncology
Pediatric Medical Director, Hemophilia and Coagulation Disorders Program
University of Michigan
Learning Objectives

• Cite the most recent clinical recommendations for the treatment of patients with hemophilia, including prophylactic factor replacement and the role of emerging agents

• Explain hemophilia-related complications associated with inhibitor development and its significant clinical and economic consequences
Hemophilia: An Inherited Disorder

- X-linked recessive bleeding disorder leading to spontaneous bleeding and bleeding following trauma or surgery
  - Typically expressed in males
  - Female carriers may be symptomatic
- Characterized by a deficiency of one or more clotting factors
  - Factor VIII (hemophilia A)
  - Factor IX (hemophilia B)

Father does not have hemophilia XY
Mother is a carrier of the hemophilia gene XX

Key
- Does not have hemophilia
- Carrier of the hemophilia gene
- Has hemophilia

50% chance sons will have hemophilia XY
50% chance daughters will be a carrier of the hemophilia gene XX

## Hemophilia: Epidemiology

<table>
<thead>
<tr>
<th></th>
<th>Hemophilia A</th>
<th>Hemophilia B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetics</td>
<td>Xq28</td>
<td>Xq27</td>
</tr>
<tr>
<td>Gender</td>
<td>99% males</td>
<td>99% males</td>
</tr>
<tr>
<td>Incidence</td>
<td>1/5,000 male births</td>
<td>1/25,000 male births</td>
</tr>
<tr>
<td>Prevalence</td>
<td>20.6/10,000 males</td>
<td>5.3/10,000 males</td>
</tr>
<tr>
<td>Age</td>
<td>Normal lifespan</td>
<td>Normal lifespan</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>72%</td>
<td>70%</td>
</tr>
<tr>
<td>African-American</td>
<td>13%</td>
<td>18%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>7%</td>
<td>5%</td>
</tr>
<tr>
<td>Other</td>
<td>8%</td>
<td>7%</td>
</tr>
</tbody>
</table>

# Clinical Classification

| Classification                  | Mild  
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(30-40% of patients)</td>
<td></td>
</tr>
<tr>
<td>Factor VIII or factor IX activity</td>
<td>&gt;5 to &lt;40% of normal</td>
</tr>
<tr>
<td>Pattern of bleeding episodes</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Cause of bleeding episodes</td>
<td>Major trauma/ surgery</td>
</tr>
</tbody>
</table>
|                                | Moderate  
| (10% of patients)             |       |
| Factor VIII or factor IX activity | 1 to 5% of normal |
| Pattern of bleeding episodes   | ~4 to 6 per year |
| Cause of bleeding episodes     | Minor trauma |
|                                | Severe  
| (30-40% of patients)          |       |
| Factor VIII or factor IX activity | <1% of normal |
| Pattern of bleeding episodes   | ~2 to 4 per month |
| Cause of bleeding episodes     | Spontaneous |

Evolution of Hemophilia Treatment

- **Low-purity pd concentrates**: Mid 1960s
- **Intermediate-purity concentrates**: 1970s
- **rFVIII available**: Early 1980s
- **High-purity concentrates**: Mid 1980s
- **Manufacturing changes for rFVIII product**: Late 1980s
- **rFIX available**: Early 1990s
- **Extended half-life factor VIII and IX**: Late 2000s
- **Today**
## Hemophilia Care Management: Treatment Goals, Approach, and Strategies

<table>
<thead>
<tr>
<th>Goals</th>
<th>Approach</th>
<th>Strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Rapid and effective replacement of missing coagulation factor:</td>
<td>Comprehensive hemophilia treatment center (HTC) staffed by a multidisciplinary team of experts who care for patients with bleeding disorders</td>
<td>• Episodic or “on-demand” factor replacement</td>
</tr>
<tr>
<td>– Bleed prevention: decrease frequency and severity of bleeding</td>
<td></td>
<td>• Prophylaxis</td>
</tr>
<tr>
<td>– Raise factor levels</td>
<td></td>
<td></td>
</tr>
<tr>
<td>– Prevent the complications of bleeding</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Hemophilia Treatment Options

Replacement of missing clotting protein
- Hemophilia A (plasma-derived and recombinant FVIII products)
- Hemophilia B (plasma-derived and recombinant FIX products)

Desmopressin acetate (DDVAP)/Stimate
- Synthetic vasopressin analog used in many patients with *mild* hemophilia A for minor bleeding and before and after surgery

Adjunctive therapies
- Antifibrinolytic agents
- Supportive measures including immobilization and rest, ice, compression, elevation (RICE)

### Factors VIII and IX

<table>
<thead>
<tr>
<th></th>
<th>FVIII</th>
<th>FIX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous infusion</td>
<td>![Check mark]</td>
<td>![Check mark]</td>
</tr>
<tr>
<td>(either IV push or</td>
<td></td>
<td></td>
</tr>
<tr>
<td>continuous)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose</td>
<td>20-50+ units/kg body weight</td>
<td>40-100+ units/kg body weight</td>
</tr>
<tr>
<td>Half-life</td>
<td>8-12 hours</td>
<td>18-24 hours</td>
</tr>
<tr>
<td>Average change in plasma</td>
<td>+2%</td>
<td>+1%</td>
</tr>
<tr>
<td>factor activity with</td>
<td></td>
<td></td>
</tr>
<tr>
<td>each unit/kg infused</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Hemophilia Management Challenges

**Early, accurate diagnosis and family history**
- Spontaneous mutation occurs in 30% of patients

**Early, adequate factor replacement for bleeding**
- Reactive, invasive, costly, does not prevent joint disease

**Prophylaxis**
- <50% of adults engage in prophylactic treatment
- Identification of optimal trough levels
- Peri-surgical considerations

**Inhibitor formation**
- Genetic predisposition
- Associated with high morbidity

## Prophylaxis Protocols*

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Definition</th>
</tr>
</thead>
</table>
| Primary prophylaxis             | • Regular, continuous† treatment initiated in the absence of documented joint disease  
                                 | • Need determined by physical examination and/or imaging studies  
                                 | • Started before the second clinically evident large joint bleed and 3 years of age‡ |
| Secondary prophylaxis           | • Regular, continuous† treatment started after ≥2 bleeds into large joints‡ and before the onset of joint disease documented by physical examination and imaging studies |
| Tertiary prophylaxis            | • Regular, continuous† treatment started after the onset of joint disease documented by physical examination and radiographs of the affected joints |
| Intermittent (“periodic”) prophylaxis | • Treatment to prevent bleeding for periods not exceeding 45 weeks in a year                                                                 |

*World Federation of Hemophilia definitions

†Continuous is defined as the intent of treating for 52 weeks/year and receiving a minimum of an a priori defined frequency of infusions for at least 45 weeks (85%) of the year under consideration

‡Large joints = ankles, knees, hips, elbows, and shoulders

## Benefits and Challenges of Prophylaxis in Severe Hemophilia

### Benefits
- Reduces joint bleeds
- Reduces joint damage (assessed by MRI)
- Prevents disability

### Challenges
- Requires frequent factor administration
- Adherence
- Invasive, may require port access
- Reimbursement

### Table: Prophylaxis in Severe Hemophilia

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Children</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early start as primary prophylaxis now standard of care</td>
<td>• Early start as primary prophylaxis now standard of care</td>
<td>• Can be continued when started in childhood to maintain healthy joint function</td>
</tr>
<tr>
<td>Recommended for patients with increased bleeding frequency</td>
<td></td>
<td>• Recommended for patients with increased bleeding frequency</td>
</tr>
</tbody>
</table>

New and Emerging Therapeutics

- Extended half-life (EHL) products allow for fewer infusions, longer protection
- Several EHL FVIII and FIX factor replacement products have been recently approved and several more are expected in the next few years
  - Safe, well tolerated
  - Improved half-life, recovery; delayed clearance
  - Efficacy comparable to rFVIII, rFIX
  - Safety comparable to rFVIII, rFIX

Sustained Factor Levels >1% Can Be Achieved With Extended Half-Life Products

- Sustained FVIII level >1% in adults receiving rFVIIIFc 50 U/kg q5d was associated with continued protection against bleeds

## New and Emerging Hemophilia Treatment Options

<table>
<thead>
<tr>
<th>Agent</th>
<th>Manufacturer</th>
<th>Description</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Factor VIII Products</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AFSTYLA (rVIII-Single Chain)</td>
<td>CSL Behring</td>
<td>rFactor VIII</td>
<td>Approved May 2016</td>
</tr>
<tr>
<td>KOVALTRY</td>
<td>Bayer</td>
<td>rFactor VIII</td>
<td>Approved March 2016</td>
</tr>
<tr>
<td>ADYNOVATE</td>
<td>Baxalta, part of Shire</td>
<td>rFactor VIII, long-acting</td>
<td>Approved November 2015</td>
</tr>
<tr>
<td>NUWIQ</td>
<td>Octapharma</td>
<td>rFactor VIII</td>
<td>Approved September 2015</td>
</tr>
<tr>
<td>ELOCTATE</td>
<td>Biogen</td>
<td>rFactor VIII, long-acting</td>
<td>Approved June 2014</td>
</tr>
<tr>
<td>NovoEight (turoctocog alfa)</td>
<td>Novo Nordisk</td>
<td>rFactor VIII</td>
<td>Approved October 2013</td>
</tr>
<tr>
<td>N8-GP (turoctocog alfa pegol)</td>
<td>Novo Nordisk</td>
<td>rFactor VIII, long-acting</td>
<td>Phase 3</td>
</tr>
<tr>
<td><strong>Factor IX Products</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IDELVION</td>
<td>CSL Behring</td>
<td>rFactor IX, long-acting</td>
<td>Approved March 2016</td>
</tr>
<tr>
<td>IXINITY (trenonacog alfa)</td>
<td>Emergent BioSolutions</td>
<td>rFactor IX</td>
<td>Approved April 2015</td>
</tr>
<tr>
<td>ALPROLIX</td>
<td>Biogen</td>
<td>rFactor IX, long-acting</td>
<td>Approved March 2014</td>
</tr>
<tr>
<td>RIXUBIS</td>
<td>Baxalta, part of Shire</td>
<td>rFactor IX</td>
<td>Approved June 2013</td>
</tr>
<tr>
<td>N9-GP (nonacog beta pegol)</td>
<td>Novo Nordisk</td>
<td>rFactor IX, long acting</td>
<td>BLA submitted</td>
</tr>
</tbody>
</table>
## Inhibitors: Definition and Prevalence

| **Definition** | Polyclonal allo-antibodies to the infused replacement factor\(^1\)  
|                | Neutralize the procoagulant effect of the infused factor as well as naturally produced factor protein\(^1\) |
| **Prevalence** | Develop in ~15-20% of patients; greater prevalence in hemophilia A (~30%) vs hemophilia B (2-5%)\(^1\) |
| **Age of Onset** | Typically develop early in life (median age 1.7–3.3 years)\(^1\) |
| **Burden** | Associated with high healthcare resource utilization (factor use, hospitalization, etc) and significant mortality\(^2\) |

Risk for Inhibitor Development by Mutation Type

Risk Factors for Inhibitor Development

- **Genetic**
  - Factor deficiency
  - Disease severity
  - Hemophilia gene defect
  - Family history of inhibitor
  - Race/ethnicity: people of African or Hispanic ancestry have a 2x greater risk
  - Immune response and modifying genes

- **Treatment-related**
  - Frequency and intensity of exposure to factor products
  - Type and structure of product used (SIPPET trial)
  - Greatest risk for inhibitor development occurs within the first 50 exposures to infused product

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Managing Inhibitors: Bypassing Agents

- Bypassing agents are often required to produce clotting in patients with significant inhibitor development
  - FVIII impractical and ineffective if Bethesda Units (BU) >5
- Products available:
  - Activated prothrombin complex concentrate (aPCC)
  - Recombinant FVIIa
- Limitations include their unpredictable efficacy and lack of laboratory monitoring
Managing Inhibitors: Immune Tolerance Induction

- Immune Tolerance Induction (ITI)
  - Regular infusions of factor VIII or IX administered for a period of weeks to years in an effort to increase the tolerance of the immune system
  - Limitations include variable efficacy (70-85% for FVIII and ~30% for FIX)
  - Time-consuming and expensive

| Dosing ITI |
|---------------------|---------------------|
| **High titer inhibitors (≥5 BU)** | **Low titer inhibitors (<5 BU)** |
| • High-dose regimen  |
| • 100-200 IU kg⁻¹ day⁻¹ | • Either with high- or low-dose regimen |
| | • 50 IU kg⁻¹, 3x/week |

Factors Associated With Successful ITI

- Initiating ITI when inhibitor levels are <10 BU/mL and ideally <5 BU/mL
- Initiating ITI within 5 years of inhibitor diagnosis
- Patients whose peak inhibitor levels have never reached >200 BU/mL and have ideally stayed <50 BU/mL
# Emerging Agents for the Management of Hemophilia and Inhibitors

<table>
<thead>
<tr>
<th>Agent</th>
<th>Description</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Novel Therapies for Hemophilia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concizumab</td>
<td>Tissue factor pathway inhibitor (TFPI)</td>
<td>Phase 2</td>
</tr>
<tr>
<td><strong>Treatment of Inhibitors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LR769</td>
<td>rFVIIa</td>
<td>Phase 3</td>
</tr>
<tr>
<td>CSL689</td>
<td>rFVIIa-FP</td>
<td>Phase 2/3</td>
</tr>
<tr>
<td>ACE910</td>
<td>FVIIa-mimetic bispecific antibody</td>
<td>Phase 2/3*</td>
</tr>
<tr>
<td>ALN-AT3</td>
<td>siRNA knockdown of antithrombin</td>
<td>Phase 2/3</td>
</tr>
<tr>
<td>Factor VIIa-CTP</td>
<td>rVIIa-CTP, long-acting</td>
<td>Phase 2</td>
</tr>
</tbody>
</table>

*breakthrough therapy designation
Preventing Bleeding in Individuals With an Inhibitor: Rationale for Prophylaxis

• Patients with inhibitors are at increased risk for difficult-to-control bleeding and complications; therefore, bleed prevention or reduction is of critical importance\(^1,2\)

• FVIII prophylaxis can prevent joint hemorrhage and subsequent arthropathy, target joint bleeds, and disability\(^3-5\)
  • Recommended by MASAC, WFH, and WHO as optimal therapy for persons with severe hemophilia without inhibitors\(^6-8\)
  • Prophylactic treatment may also improve health-related quality of life (HRQoL)\(^9-11\)

Pro-FEIBA: Study Results

• In comparison to aPCC on-demand treatment, aPCC prophylaxis 85 U/kg ±15% given on 3 nonconsecutive days weekly...

Reduced all bleeding by 62% (P<0.001)
Reduced joint bleeding by 61% (P<0.001)
Reduced target joint bleeding by 72% (P<0.001)

aPCC = activated prothrombin complex concentrate (FEIBA®)
PROOF Study Results

• In comparison to aPCC on-demand treatment, aPCC prophylaxis 85 U/kg ±15% given every other day...

  Reduced median ABR for all bleeds by 72.5% (P=0.0003)

  Reduced median ABR for joint bleeds by 73.8% (P=0.0006)

  Reduced median ABR in new target joints* by 100% (P=0.0271)

*Ankles, knees, elbows, and/or hips with ≥4 bleeds over 6 months

aPCC = activated prothrombin complex concentrate (FEIBA™)
ABR = annual bleed rate
Prophylaxis With aPCC in Pediatric Patients With Hemophilia A and Inhibitors

- aPCC prophylaxis in pediatric patients decreased the annual number of joint bleeds by a mean of 85.4% the first year ($P=0.0179$) and improved joint status.

aPCC = activated prothrombin complex concentrate (FEIBA®)

Dilemmas Encountered When Treating Hemophilia With Inhibitors

• Treating and preventing bleeds
  • No universally effective agent
    • Activated prothrombin complex concentrates (aPCC) work for some bleeds, but not all
    • rFVIIa works for some bleeds, but not all
  • No laboratory test that accurately predicts or confirms hemostasis
  • rFVIIa has short half-life, needs frequent infusions

• Inducing immune tolerance
  • Not effective in one-quarter to one-third of patients
  • The role of or need for von Willebrand factor in preventing and clearing inhibitors is uncertain
  • Immune suppression/modulation (ie, anti-CD20 agents) is variably effective and may be temporary
• Hemophilia treatment goals include rapid and effective replacement of missing coagulation factor to prevent and/or decrease the severity of bleeding and prevent bleeding-related complications

• Inhibitors and prophylaxis considerations represent two of the greatest clinical challenges in the treatment of hemophilia
  • Aggressive and vigilant therapeutic intervention is crucial to success and the minimization of morbidity/mortality
  • Emerging therapeutics in the form of extended half-life agents and therapies with novel mechanisms of action present promising options for the advancement of prophylaxis and the management of inhibitors
Strengthening the Value of Managed Care and Specialty Pharmacy for Successful Management of Hemophilia

This activity is supported by independent educational grants from Alnylam Pharmaceuticals, Shire, Bayer HealthCare Pharmaceuticals, Grifols, and Novo Nordisk, Inc.
Optimizing the Pre-Certification and Prior Authorization Processes

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Vice President, Ambulatory Clinical Pharmacy Programs_PCM
Henry Ford Health System/Health Alliance Plan of Michigan
Learning Objective

• Apply methods to enable optimal cost management of factor replacement therapy to be realized by managed care organizations (MCOs) and specialty pharmacy providers
What Is Prior Authorization?

• Prior authorization (PA) is a prospective process to verify coverage criteria of proposed care have been met
• Also used as cost-saving feature to ensure the safe and appropriate use of selected drugs
• Criteria based on clinical guidelines and medical literature
• PA criteria vary by payer and product line

What Is Pre-Certification?

• Pre-certification is similar to PA—an administrative procedure used by a payer to authorize treatment before it is provided

• Under many plans, pre-certification is required before hospital admissions, inpatient or outpatient surgeries, and elective procedures

• Emergencies are usually exempt

Prior Authorization Submission Process

1. Verify Benefits
2. Collect Information
3. Submit Request
4. Prior Authorization Decision
5. Appeals (if needed)
Prior Authorization Submission Process:
Verify Benefits

- Verify eligibility and medical policy requirements
- Verify physician and facility contract network status with payer
- Verify payer requirements for prior authorization
Prior Authorization Submission Process: Collect Information

- Patient information
- Plan type
- Insurance number
- Contact information
- Diagnosis code(s)
- Office notes
- History and physical exam
- Statement of medical necessity
Prior Authorization Submission Process: Submit Request

- Obtain payer’s PA form for replacement factor
- Complete required forms
- Attach clinical documentation to support use of restricted drug
- Attach published literature to support drug criteria variance
- Submit drug request
Prior Authorization Submission Process:
Prior Authorization Decision

- Prior authorization decision can take between 1 and 15 days depending on the product line and level of urgency
- Prior authorization decision will be sent to both provider and member
Prior Authorization Submission Process: Appeals Process

- Physician or member can submit an appeal per process outlined in denial letter
- Submit requested appeal documentation to payer
- Appeal decision can take between 3 and 30 days depending on the product line and level of urgency
Coverage for Replacement Factor

• Replacement factor can be covered as a
  • Medical benefit
  • Pharmacy benefit

• Most insurers require prior authorization for coverage

• Within health plans, coverage criteria can vary by product line (eg, Medicare, Medicaid, Commercial membership)

• Most health plans provide online coverage criteria for providers
Duration of Coverage

- Most drugs meeting coverage criteria are approved for a 1 year period.
- Drugs requiring more frequent dose titrations or closer monitoring for safety/effectiveness are reassessed more frequently.
- High factor doses required for patients with inhibitors may require monthly reviews to assure the drug and dose are being monitored closely.
- Reauthorization is required at the end of each interval.
- Failure to meet prior authorization criteria at renewal time point will result in a denial of coverage for future doses.

Keep in Mind...

- Prior authorization requirements are subject to change as a result of:
  - Annual benefit modifications
  - New drugs within same class entering the market
  - New pertinent published literature findings
  - National guideline updates
Streamlining Prior Authorization Is a Top Priority for Providers and Payers

Current Gaps in PA Activities

- Prescriber not aware that prescribed drug requires PA
- PA criteria not visible to the prescriber
- PA criteria for same drug can vary by payer
- Each payer has their own PA forms
  - Some states have standardized PA forms for all payers to use
- Paper forms require manual entry with potential for error
- Routes to obtain PA are not standardized and vary depending on the health plan, drug, pharmacy, and patient situation
Current Methods of Communication Between Prescribers and Payers

**Paper-based**
- Preprinted paper forms faxed

**Telephone-based**
- Person-to-person/voicemail

**Electronic**
- Digital systems integrated into the EMR and/or other online systems
Streamlining the Process: Electronic Prior Authorization

• Electronic PA reduces administrative burden and increases workflow efficiency

Advantages of Electronic Prior Authorization

• Leverages eligibility and formulary data to notify providers of PA requirements before prescribing
• PA questions are sent to the electronic health record (EHR), based on patient, plan, and medication
• Pre-population of required patient information adds efficiency and accuracy to administrative tasks
• Real-time communications with payer (eg, PBM) to complete PA review before sending the prescription to the pharmacy
• Preapproved prescriptions routed to pharmacy
• Minimizes delays in medication delivery to the patient

Caveat: Electronic Prior Authorization Implementation Varies Across Prescriber and Payer Practice Settings

<table>
<thead>
<tr>
<th>Capability</th>
<th>Prescriber Portal</th>
<th>Payer Portal</th>
<th>Fully Integrated</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Integrated into physician EHR workflow</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>• Prospective workflow capabilities</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>• Retrospective workflow capability</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>• Integrated into the e-prescribing workflow</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>• Automatically pull patient medical history from EHR into PA question set</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>• Broad connections to several PBMs/payers</td>
<td>✓</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>• Bi-directional network of PBM/payers and providers/EHRs</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

Summary

• Prior authorization is used to verify coverage of proposed care and ensure the safe and appropriate use of selected drugs

• The PA process includes collecting patient information, verifying patients’ health insurance benefits, submitting the required forms, and filing an appeal if denial reason is not supported clinically

• Streamlining the PA process is a top priority for many payers

• Many payers and practice settings are implementing systems that integrate the EHR, e-prescribing tools, and the PA process to prospectively receive approval prior to sending the prescription to the pharmacy for filling

• While promising, the impact of these systems is currently limited by a lack of standardization and the cost of development, implementation, and training
Strengthening the Value of Managed Care and Specialty Pharmacy for Successful Management of Hemophilia

Satellite Symposium held in conjunction with AMCP Nexus 2016

This activity is supported by independent educational grants from Alnylam Pharmaceuticals, Shire, Bayer HealthCare Pharmaceuticals, Grifols, and Novo Nordisk, Inc.
Hemophilia Treatment Center and Specialty Pharmacy Collaboration: Steps for Success

Michael Zeglinski, RPh
Senior Vice President, Specialty Pharmacy
OptumRx®/BriovaRx®
Learning Objective

• Identify processes for managed care organizations (MCOs) and specialty pharmacy providers to improve communications with hemophilia treatment centers (HTCs)
Improvements in Therapy Have Increased Life Expectancy of Patients With Hemophilia

- Costs will rise as patients live longer

Role of Hemophilia Treatment Centers

- Coordinate state-of-the-art medical treatment across the lifespan, including the coordination of dispensing factor
- Education
- Research
- Outreach
- Psychosocial support services
- Ensure optimal therapy for patient (age, activity level, medical background)
- Prepare patient and families for at-home treatment

HTCs provide care for patients irrespective of insurance status
Hemophilia Treatment Center Is a Collaborative Team of Hemophilia Experts

Core team members
- Patient/family
- Hematologist
- Nurse
- Social worker
- Physical therapist

Additional team members
- Other physicians
  - Primary care
  - Orthopedics
  - Infectious disease
  - Obstetrics-gynecology
  - Hepatology
- Pharmacist
- Geneticist
- Dentist
- Nutritionist
- Educational/vocational counselors
Benefits of Comprehensive Care

- Use of hemophilia treatment center services is associated with
  - Greater use of and adherence to home therapy regimen
    - 61% of patients perform home therapy if they visit an HTC vs 25% of those who do not\(^1\)
  - 40% fewer hospitalizations for bleeding complications observed\(^2\)
  - 40% fewer deaths despite HTCs seeing a greater number of patients with severe complications (HIV/AIDS, hepatitis, etc)\(^1\)

Hemophilia Treatment Center Care Minimizes Hospitalizations for Bleeding Complications


HBC = hospitalization for bleeding complications
Evolving Role of Specialty Pharmacy

Manage Patient
- Access to services
- Holistic care model

Manage Outcomes
- High-quality care focus
- Adherence

Manage Payer
- Control spend
- Demonstrate quality care services
- Network requirements

Key Components of Specialty Pharmacy Care in Management of Hemophilia

- Coordination with prescribing physicians, HTC staff, and home health care
- Patient education and follow-up for adherence and appropriate administration
- Appropriate dosing on weight and/or assays
- Dispensation in accordance with specific deviation ($\pm 10\%$); when possible, set a goal of $\pm 5\%$
Specialty pharmacy providers may offer different areas of expertise as well as varying geographic capabilities and services:

**Full-service specialty pharmacies**
- Support several chronic specialty conditions and may or may not have disease-specific areas of expertise

**Hemophilia specialty pharmacies**
- Focus exclusively on serving patients with bleeding disorders and possible comorbidities

**Advanced therapy specialty pharmacies**
- Focus on limited specific specialty area/conditions

**Infusion specialty pharmacies**
- Focus on conditions requiring infused medications
Specialty Pharmacists Can Be Actively Involved in a High-Touch Program

• Before medication is delivered to a patient’s home, the specialty pharmacist should conduct the following interventions:

**Drug Utilization Evaluation**
- Confirm diagnosis, pertinent medical history, allergies, current medications, height, weight, therapeutic appropriateness, therapeutic duplication, and disease contraindication of drug/medical device used by the patient

**Assay Management**
- Current “Standards of Service” recommend dispensing of factor within ±10% of the prescribed dose; when possible, set a goal of ±5%
- Goal: dispense as close to the prescribed target dosing as possible, barring extenuating circumstances

National Hemophilia Foundation. MASAC Document #188. 2008.
Assay Prescription Management Results: Annual Trend


Lower variance drives cost down for payers

$16,920 annual savings at 2% variance compared to 10%

HTC vs Non-HTC Specialty Pharmacy Providers

**HTC Specialty Pharmacy**

- Assure minimum factor wastage due to dosing accuracy
- Tight assay management to reduce unnecessary use of higher factor doses
- Pass on drug cost savings to health plans from HTC affiliation with 340B-qualified health centers

**Non-HTC Specialty Pharmacy***

- Coordinate use of specialty pharmacy and/or home care agency
- Assure use of appropriate doses to minimize factor wastage
- HTC may not be able to confirm factor delivery or appropriate use of factor when an SPP unaffiliated with the HTC is used

*SPPs contracted by health plan to provide specialty drugs across multiple disease states
Collaboration Between Payers, HTCs, and Specialty Pharmacy Contributes to Effective Care

- Payer
- Hemophilia Treatment Center (HTC)
- Specialty Pharmacy Provider (SPP)
Specialty Pharmacy Provider Alignment With Prescribers/HTCs Can Enhance Continuity of Care

• Communication of critical data must occur before and after each clinic visit to ensure the patient’s defined “care plan” is being met

• Critical data include
  - Infusion frequency, units/assays dispensed, in-home challenges, educational deficits, etc
  - Payer and benefit information to assure compliance and avoid delays in treatment

• The level of interaction between HTC and SPP varies by facility based on available resources/needs, patient volume, and clinic preferences
## Patient Management and Support Opportunities

### Role of the HTC
- **Delivery of care**
  - Team of providers and support staff
- **Patient support services**
  - Emotional support
  - Education
  - Physical therapy
  - Financial
- **Coordinate care with**
  - Health plans
  - SPPs
  - Other resources outside the HTC

### Role of the SPP
- **Pharmacist assessment assay management**
- **Coordination with HTCs (eg, administration, adherence, etc)**
- **Coordination with health plan (eg, prior authorization, payment, etc)**
- **Patient education**
- **Identify need for referral to specialist medical provider**
- **Provision of emergency ancillary supplies as needed**

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CCSC Initiative Strives to Facilitate Payer-Provider Collaboration

• Ongoing quality improvement (QI) and cost management initiative
• Driven by the insights of a prominent group of stakeholders:
  • HTC directors, clinicians, and administrators
  • Payer/managed care medical and pharmacy directors from a mix of large national and regional health plans
• Developing a framework for metric-driven pilot programs incorporating data reporting between payers and HTCs to be replicated across the United States

**Goal:** facilitate cost-effective hemophilia management integrating the HTC comprehensive care model
Summary

• Better treatments have increased the lifespan of patients with hemophilia
• Effective management of hemophilia can improve clinical and economic outcomes
• HTCs provide state-of-the-art collaborative medical care across the lifespan, including the coordination of dispensing factor
• Treatment in an HTC is associated with greater adherence, fewer hospitalizations, and lower mortality
• SPPs are increasingly called upon to support the care of patients with hemophilia
• SPPs often work with the HTC to coordinate care, manage data, ensure appropriate dosing, provide patient education, and support patient adherence to their therapy
This activity is supported by independent educational grants from Alnylam Pharmaceuticals, Shire, Bayer HealthCare Pharmaceuticals, Grifols, and Novo Nordisk, Inc.