Market Insights 1
July 2018

Summit on Hemophilia
Findings from the AMCP Market Insights Program

Abstract
Recent therapeutic advances in hemophilia have led to a wave of new FDA-approved agents, and with it concerns of growing costs for managing the disease. By some estimates, the hemophilia category is nearly $11 billion, with signs of increasing compounded annual growth. In light of increasing specialty spend in this category, health plans are beginning to consider identifying opportunities to implement care optimization and cost management strategies. However, due to the complexity of treatment and the current care models, health plans need to understand the current business models in place, and the potential impact on patient care and decisions. AMCP convened an expert forum of stakeholders representing hemophilia treatment centers, specialty pharmacies, advocacy, clinicians, and health plans to discuss the current patient care and business models in delivering care to members with hemophilia in an effort to identify areas for more efficient care delivery. Participants discussed coverage and reimbursement models in hemophilia, cost drivers, coordination of care, and recommendations for implementing changes in care delivery to manage rising costs.

Meeting Objective
• Understand current care models supporting hemophilia today.
• Strategies and new approaches to care management and coordination among stakeholders.

Introduction
Hemophilia is a rare, inherited, lifelong bleeding disorder, affecting mostly males. The current market is estimated at $10.9 billion—with a compounded annual growth rate (CAGR) of 6.0%. As a category, it represents a significant resource utilization for health plans despite a low disease prevalence of 0.01% of the total U.S. population. Per-patient/per-year cost remains significant, at an average of $155K-$161K, and as high as $2.5 million for patients with severe disease and/or inhibitors. Hemophilia accounts for roughly 3% of the typical health plan mix. For employers, it ranks 8th in spending across specialty diseases. Contributing to costs beyond treatment are emergency room (ER) visits, suboptimal care coordination among stakeholders, lack of patient adherence to prescribed therapy (referred to as “factor”), and a population with growing longevity.

A primary driver of the market growth stems from a highly competitive landscape with new FDA approvals, and newer formulations expected over the next several years. In fact, nearly 60 compounds are in various phases of clinical development, 15 of which represent first-in-class molecules. According to hemophilia treatment centers (HTCs), the majority of hemophilia patients are covered through private plans (51%) or Medicaid (30%); the remaining mix is comprised of Medicare, other types of coverage, and the uninsured. The current care delivery model for patients with hemophilia is established through coordination of primary care providers, HTCs, and specialty pharmacy providers (SPPs). Thus, most health plans do not currently restrict provider type and site of care, leaving an open network of care for their members with hemophilia.

“Cost drivers include ER visits, poor care coordination, patient adherence, and a population with growing longevity.”
AMCP Market Insights Program

Despite changes in the marketplace and growing costs, health plans currently do not aggressively manage the hemophilia category. To do so, plans need to understand existing care delivery models in hemophilia so that any potential management or restrictions are made with knowledge of care and how members may be impacted. To understand this, AMCP conducted a Market Insights program consisting of a live forum of key stakeholders to understand and evaluate current care management and business models supporting hemophilia care. These included HTCs, (SPPs), clinicians involved in the care of patients with hemophilia, and health plans (government, commercial, and PBMs). Discussions focused on models of care coordination, patient services, cost considerations, and recommendations for future management of hemophilia.

Cost drivers for individual type of patients signal a concern for managing the category

In a pre-meeting survey, health plans noted that they expect management to increase significantly (4.29/5-point scale). This is expected, as hemophilia does not fit the typical 2-5 year membership enrollment churn observed for insured patients in other therapeutic categories, requiring an approach to manage these members with a longer-term perspective. Participants point to a range of cost issues they consider in evaluating hemophilia products. Specifically, SPPs and HTCs report that unit price of factor (i.e., essential blood-clotting protein) and use alone are not the sole attributes in considering cost of patient care.4 Other considerations include newer agents with extended half-life, which are more expensive but may allow patients the ability to benefit from a more effective prophylactic treatment option. Additionally, a growing population of members, largely driven by increasing longevity with co-morbidities and complications, are likely to further fuel costs.

“Unit price…and use alone are not the sole attributes in considering cost of patient care.”

Importantly, health plans currently view costs in aggregates of factor units, and not by individual attributes such as age, “on-demand” versus prophylaxis use, inhibitor treatment, type of patient, or adherence. Furthermore, because they are unaware of which members are treated with on-demand or prophylaxis treatment, they are unable to assess patient variability. Recognizing the differences in usage among populations can serve as an opportunity to optimize individual patient care and manage overall costs.

“Health plans currently view costs in aggregates of factor units, and not by individual attributes such as age, on-demand versus prophylaxis use, inhibitor treatment, type of patient, or adherence.”

Another key variable in cost is disease severity and amount of factor replacement.4 While mild patients, who usually treat on-demand to manage spontaneous bleeds, have the lowest factor utilization and cost, severe patients receiving prophylaxis treatment comprise the segment with highest costs.4 The costliest patients to a health plan are those who develop inhibitors—which can contribute significantly to annualized costs for product, at estimated $721,603 across hemophilia A or B patients, based on Medicare Average Sales Price (Figure 1).6 The development of inhibitors is one of the most serious complications of hemophilia7 and carries with it significant cost for treatment. Inhibitors most often appear during the first 50 times a person is treated with clotting factor, but they can appear at any time.8 Patients who develop inhibitors are characterized by a tolerance to factor. As a result, their inhibitor prevents effective use of replacement factor.9 Such patients may require different treatment options: (1) immune tolerance induction (ITI) therapy and variable dose of replacement factor, (2) bypassing agents to treat bleeding in those presenting with a high level of inhibitors, or (3) a combination of these.9,10

“Recognizing the differences in usage among populations can serve as an opportunity to optimize individual patient care and manage overall costs. This is a missed opportunity to better manage both care and cost.”
Importantly, assay management represents a significant and growing concern related to appropriate dose and frequency, wastage and inventory. Assay management refers to the appropriate amount of factor prescribed and utilized by patients. Unlike with traditional prescriptions, providers may prescribe factor for hemophilia in ranges, which may vary from patient to patient. As an example, one adult patient with hemophilia A may be prescribed a prophylactic dose of “2,000 units ± 10%, 3x weekly,” whereas another adult patient may be prescribed “1,500-1,700 units, 3x weekly.” The reason for such broad dose variability is to allow members to have access to factor in the event of spontaneous bleeds or unexpected bleeds between infusions. Although these differences in prescribed assays may be attributed to disease severity, patient weight, and manufacturer label, managing their utilization is a challenge if a health plan is trying to control overall dispensing.

**Site of care plays a role in assay management**

Unit cost is particularly concerning, as it varies by site of care. Generally, most patients with hemophilia self-infuse at home with factor shipped or provided through an HTC pharmacy or SPP. However, patients may present at the ER with unexpected bleeds and without product availability to administer. In such cases, hospitals administer the factor stocked at their on-site pharmacy. Those who are admitted for complications and ongoing bleeds represent an additional cost—partly driven by hospital charges for factor as well as inpatient services provided. There is broad consensus among participants that patients who keep inventory of factor at their homes can minimize ER visits, since they can carry their own prescribed product when presenting at the hospital for bleeds. Policy on administering the patient’s own prescribed product may vary from hospital to hospital, as some may have diagnosis-related

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*Costs are similar for members with hemophilia A and B.*

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**Figure 1. Annualized Factor Costs by Disease Severity, Including On-Demand vs. Prophylaxis Use**

<table>
<thead>
<tr>
<th>Disease Severity</th>
<th>Number of Members</th>
<th>Annual Per Patient Costs ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild (n = 74)</td>
<td>$42,167</td>
<td></td>
</tr>
<tr>
<td>Moderate (n = 35)</td>
<td>$62,7870</td>
<td></td>
</tr>
<tr>
<td>Severe (episodic) (n = 67)</td>
<td>$159,761</td>
<td></td>
</tr>
<tr>
<td>Severe (prophylaxis) (n = 123)</td>
<td>$275,324</td>
<td></td>
</tr>
<tr>
<td>Inhibitor (n = 16)</td>
<td>$721,603</td>
<td></td>
</tr>
</tbody>
</table>

*Costs are similar for members with hemophilia A and B.*

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“The development of inhibitors is one of the most serious complications of hemophilia and carries with it significant cost for treatment. Health plans may be aware of members who have inhibitors, but rarely have a plan in place to manage them.”
group (DRG) codes to accommodate what is referred to as “brown bagging” of patient factor. At the same time, other hospitals will naturally want to absorb the infusion cost and control the distribution channel.

“Due to prescribing variances, health plans can conduct audits on prescribed versus dispensed factor to gain a better understanding of appropriate utilization.”

Patient stockpiling of product at home nevertheless remains a hot button issue. It represents a valid concern for health plans because patients who maintain inventory at their homes do so out of fear from having lived through shortage, fear of spontaneous bleeds or lack of insurance. Participants in the forum perceived that patients may have access to more factor than they need. This can be exacerbated by product shipping inefficiencies (such as monthly auto-shipments). Generally, while prescriptions cite a dose margin of ±10%, some health plans place tighter controls on dose margins (3%).

Some participants suggest that SPPs as well as HTCs pharmacies can take a proactive role in monitoring refills of prescriptions as well as auditing home inventory. This can be done through electronic records as well as manual phone calls and e-mails. Such practices underscore the opportunity to minimize wastage by reviewing and approving prescribed factor that is paid per script.

“SPPs and HTCs can take a proactive role in monitoring refills of prescriptions as well as auditing home inventory to minimize stockpiling.”

Guidelines and a clear algorithm remain under the radar

While participants recognize the value of guidelines, there is little awareness among health plans and pharmacy benefit managers (PBMs) of guidelines developed by the National Hemophilia Foundation’s Medical and Scientific Advisory Council (MASAC). MASAC is composed of physicians, scientists and other medical professionals with a wide range of expertise on bleeding disorders, blood safety and infectious disease. According to the National Hemophilia Foundation (NHF), MASAC establishes these standards annually, which are “often referred to by international experts, medical schools, pharmacists, emergency room personnel, insurance companies,” and others. Other recommended models endorsed by the American Society of Hematology include the NHF-McMaster Guidelines. These were developed to identify best practices in hemophilia care delivery that can optimize outcomes. Specifically, these guidelines provide evidence for applying the integrated care model for patients with or at risk for developing inhibitors. HTCs report that this model has led to a reduction in outcomes-related cost, with one estimate at a 40% reduction in mortality and hospitalization risk.

“There is a lack of awareness among health plans of national guidelines, despite endorsement by clinical organizations such as American Society of Hematology.”

With an expanding list of new products, health plans look to rely on outside input and recommendations to inform their decisions. However, a gap remains in health plans’ knowledge of evidence-based value frameworks. For example, only a minority of participants were aware of a recent Institute for Clinical and Economic Review (ICER) publication on hemophilia, specifically on the cost effectiveness of emicizumab. Such third-party opinions may help drive clarity around cost-effectiveness and relevant metrics for outcomes. In the absence of such guidance, health plans have noted that they have reviewed new products without restrictions beyond prior authorization. For it to be effective in decision making, cost-effectiveness data would need to be timely and defensible.

Emerging integration of HTC and SPP entities in care coordination

The interaction between HTCs, health plans, and SPPs is of particular significance in the evolution of hemophilia care coordination. Traditionally, the roles of these entities have been clearly demarcated. The health plan provides patient coverage and provider reimbursement; the HTC provides provision of integrated care, dispensation of factor, and assay management; and the SPP dispenses product while monitoring adherence and fulfillment. Today, the distribution mix is comprised of 60% for specialty pharmacy/home, 30% at HTCs, and 10% at hospitals.
Hemophilia Treatment Centers

The majority of health plans have open contracts with specialty pharmacies and HTCs. Most HTCs are federally recognized as 340B entities. This eligibility allows the centers to purchase product at a discounted price. Revenue from 340B-eligible HTCs supports integrated care coordination, unbilled ancillary services, and staffing for outpatient and follow-up visits. A significant but lower percentage of funding is allocated toward operating expenses (rent, utilities, etc.). Despite this, HTCs report that they continue to absorb their own cost and claim not to bill for the most expensive clinical services, charging only for physician office visits and lab work.

In addition, centers may also benefit from separate federal funding to support educational programs, research initiatives, and to deliver high-touch patient coordination. However, this additional funding, on average about $35,000 annually and is inadequate to fully support HTC services. HTCs also note that their care integration is coordinated with PCPs, through online educational programs that target providers outside of network.

HTCs adopt a thorough approach to care coordination: The HTC Comprehensive Care Model aims to address physical, emotional, psychological, educational, financial and vocational needs of patients. This model is unique to HTCs because they train providers on site through ongoing care coordination, utilize data to assess cause of bleeds, and work to identify psychosocial issues that may help prevent poor outcomes. Importantly, HTCs devise annual treatment plans with preventative medicine. In doing so, they adopt a comprehensive care model that is designed to achieve cost avoidance and enable access to multiple specialties and disciplines.

Outcomes-related benefits of HTCs include integrated care coordination, unbilled ancillary services, and staffing for outpatient and follow-up visits.

“Revenue from 340B-eligible HTCs supports integrated care coordination, unbilled ancillary services, and staffing for outpatient and follow-up visits.”
Specialty Pharmacy Providers

Specialty pharmacies represent a stakeholder with established ability to aid in identifying cost triggers and managing costs. Today, many have expanded their services with broader benefits to cover three core areas of service: clinical, financial and outreach.

Clinical
- **Completing assessments by hemophilia experienced clinicians.** Historical frequency and location of bleeds, type of IV access, presence of inhibitors, and weight
- **Review of prescribed medication.** Clarifying patient diagnosis, utilization of units/kg, and comparison of dose to MASAC and/or prescribing information
- **Re-assessments.** Number of bleeds since last contact, doses on hand, reconciliation of remaining doses, reported ER/Hospitalization, and upcoming procedures

Financial
- **Assay management.** Percent variance from the prescribed dose, broad inventory required for assay selection, and appropriate prescribed dose
- **Economic assessment.** Reconciling inventory in home, quarterly utilization and claim trends, Identification of outliers and expected utilization changes, pipeline updates, and collaboration with third-party health plans

Outreach
- **Communications.** Monitoring of reported bleed, adherence to plan, home visits to monitor usage and identify potential stockpiling, identification of barriers to optimal outcomes, demographic needs assessment, tools audit, and collaboration with HTC or prescribing HCP
- **Utilization assessment.** Evaluation of consistency with expectations for factor dispensed

The broad range of offerings by SPPs presents a challenge for cost-effective utilization of services. With an increase in shifts of specialty products to the pharmacy benefit, SPPs now have greater ability to review claims and monitor home utilization, bleeds, and joint health in patients with hemophilia. In contrast to HTCs, they are not 340B-covered entities; however, some have already begun to partner with HTCs to support their patients. Thus, long-standing agreements to provide and pay for patient services between SPPs and manufacturers may further support the additional care provided for patients.

What does the future hold?

Participants recognized that with open networks and patient variability there are few, if any, standards or metrics to assess quality of care. Accordingly, they advocate development and implementation of a standardized scorecard that health plans can review to evaluate metrics for patient care across providers. Specifically, they all seek clinical data sharing between HTCs, SPPs and health plans to better measure outcomes among health systems. Although not all services may always be required (as with emicizumab subcutaneous formulation), the need for assay management and monitoring may still be needed to evaluate micro bleeds and joint health.

“Open networks and patient variability reveal no standards or metrics to assess quality of care.”

With regard to contracting, health plans anticipate increased scrutiny to stem cost and budget impact (Figure 3). Two noted examples include the formulary rebate and the market share rebate.

1. In the formulary rebate scenario, manufacturers would pay customers through an “Access Rebate,” represented by the quarterly total net aggregate of factor.
2. In the “Market Share Rebate” option, the percentage of market share drives the formula.

In either formulation, utilization of factor is the driving variable. Participants advocated for all stakeholders meeting periodically to review charts of individual patients and understand the specific costs associated with their care.

Summary

Participants were asked to break in to groups, separated by HTCs, SPPs and health plans. Groups were asked by channel to identify opportunities, other than manufacturer rebates, that might optimize delivery of care and manage costs. Table 1 outlines participant recommendations.

The future of hemophilia management brings cautious change and prescriptive recommendations. Health plans will continue to set prior authorizations in plans, but the greatest shift signals a change in how decision makers will manage the disease based on total cost of care, product utilization, and patient outcomes.
Table 1. Stakeholders’ Needs for Implementing Change in Hemophilia Care and Cost Management

<table>
<thead>
<tr>
<th>Health plans</th>
<th>SPP</th>
<th>HTC</th>
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<tbody>
<tr>
<td>• Risk-sharing contracts with HTCs</td>
<td>• Leverage case managers and open dialogue with health plans</td>
<td>• Greater contracting between HTC and SPP pharmacies and health plans for shared savings model</td>
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<tr>
<td>• Hemophilia centers of excellence</td>
<td>• Collaborate with plans about utilization and individual member evaluation</td>
<td>• Reimbursement model that includes SPP for their services</td>
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<tr>
<td>• Claims analysis and modeling based on meta-analysis of range of products</td>
<td>• Geo-mapping access to help identify patients that can save costs through home nurses and services</td>
<td>• Outcomes data with incentives and penalties</td>
</tr>
<tr>
<td>• Standards of practice for SPPs</td>
<td>• Replace population-based approach with customized care</td>
<td>• Quarterly or annual report structure to better manage members</td>
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<tr>
<td>• New guidelines</td>
<td></td>
<td>• Consolidate multiple HTCs for efficient reporting</td>
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<tr>
<td>• Integrated patient services</td>
<td></td>
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<tr>
<td>• Information about individual patients to highlight areas of need and source of care coordination costs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Replace population-based approach with customized care</td>
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References
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5. UnitedHealth Group, 2011; UnitedHealth Center for Health Reform & Modernization.
8. CDC. Hemophilia — Inhibitors. Available at: https://www.cdc.gov/nchbddd/hemophilia/inhibitors.html.
MARKET INSIGHTS

Summit on Hemophilia

Key Summary Findings Include the Following:

- With new entrants and products with high prices, the hemophilia market is expected to grow significantly, triggering health plan management of utilization and costs.
- Assessment is likely to evolve from looking at aggregate annual product costs to identifying individual patients with greater disease severity and inhibitors and manage them on a case-by-case basis.
- Health plans struggle to identify patients treated with prophylaxis or on-demand therapy, undermining overall cost of care.
- Health plans lack guidance on measuring and assessing cost-effectiveness of available products when making coverage and formulary decisions.
- Whereas the primary metric of hemophilia cost management is IU utilization, other individual patient factors, which may contribute significantly to cost, go unnoticed and unaddressed.
- Assay management may be a key opportunity to manage utilization and reduce waste.
- Provider education and nurse services should be directed to help optimize prevention of bleeds and appropriate dosing.
- Opportunity exists to optimize care through better coordination among SPPs, HTCs and health plans; patient services offered through HTCs and SPPs should minimize overlaps of care.
- Standards of practice should be streamlined through validated models of care and clinical guidelines, such as MASAC.

How Will This Impact Your Current and Future Decisions?

When evaluating processes and procedures to optimize hemophilia treatment and costs, health plans may want to consider the following:

- How might the roles and services provided by SPPs and HTC alter your partnerships in hemophilia management?
- What opportunities do you envision for contracting with manufacturers?
- How might you alter auditing of distribution and dispensing to ensure appropriate factor and assay utilization?
- How might you implement policies to effectively identify appropriate members who can benefit from prophylaxis treatment to prevent bleeds or switching product?
- How do you envision members with inhibitors impacting your management? What plans do you have in place to manage members who develop inhibitors?
- What mechanisms are needed to share best practices in this space?