



Hemophilia and Managed Care: Partnering to Achieve Cost-Effective Care

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Educational Objectives

After participating in this educational activity, participants should be able to:

1. Differentiate hemophilia from hemophilia with inhibitors, and identify the unique challenges associated with inhibitors.
2. Evaluate the impact of changes in the treatment of pediatric and adult hemophilia on their organizations.
3. Identify opportunities to engage clinical and financial stakeholders in the medical care and management of pediatric and adult hemophilia patients, thereby increasing the effectiveness of participants in the care process.
4. Evaluate current formulary development and management techniques and specialty pharmacy arrangements, and incorporate new concepts to improve the quality and cost-effectiveness of care for both pediatric and adult hemophilia patients.
5. Better integrate available resources such as hemophilia treatment centers into clinical treatment and overall patient management.

Target Audience: This activity has been designed to meet the educational needs of medical, pharmacy, and executive leaders; quality managers; outcomes managers of payer organizations; specialty pharmacies; and others who finance and work with the hemophilia community to manage the care of patients with hemophilia.

Type of Activity: Knowledge

Disclosure Policy

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In late 2010, the Pharmacy & Therapeutics Society, with significant contribution from the National Hemophilia Foundation (NHF), convened a series of 6 educational webinars for payer executives. The primary objective of the webinars was to explore how health plans and hemophilia treatment centers (HTCs) can better work together to deliver high-quality care and manage costs associated with hemophilia. Each webinar's faculty comprised an HTC hematologist, an HTC nurse, and a managed care executive. Each webinar was part of an accredited continuing education program. These webinars were made possible by an unrestricted educational grant from Novo Nordisk.

Most of the 66 webinar attendees represented the medical and pharmacy departments from commercial, Medicaid, and Medicare health plans located across the country. The health plans were diverse, ranging from national plans with multiple lines of business to small regional plans and state Medicaid agencies. A few attendees represented pharmacy benefit managers (PBMs) and specialty pharmacies. This article is based on the educational materials presented and the discussions that transpired during the webinars.

Hemophilia is a chronic, rare disease with significant individual patient cost. Over the last few decades, with the introduction of new treatment modalities, the management of pediatric and adult hemophilia patients has progressively improved outcomes and resulted in increased longevity and decreased morbidity of disease. However, the transmission of viral blood-borne infections via replacement products (largely prior to 1990), clotting factor deficiency-associated arthropathy, and spontaneous and traumatic bleeding episodes have affected a significant segment of the hemophilic population. Overall care for bleeding-disorder patients is complex and requires an expert, dedicated multidisciplinary team. As hemophilia is a rare disorder, health plans often do not invest as many resources to evaluate formulary and coverage issues as they might for higher prevalence diseases with greater associated patient numbers and total cost.

Many webinar attendees suggested that their health plans do not fully understand the comprehensive medical and support services that HTCs provide and the positive impact those services have on patient quality of life and cost of care. Also, many webinar attendees reported that they have not fully evaluated the complexities of hemophilia and their impact on medical and pharmacy benefit design, formulary development, therapy acquisition, and patient management. Many webinar attendees believed that payers and HTCs might not have fully explored appropriate avenues to productively work together.

As this article demonstrates, a closer working relationship and better mutual understanding between health plans and HTCs could improve outcomes for hemophilia patients while providing a more favorable cost-to-benefit ratio. Treatment of rare diseases like hemophilia is unlikely to result in cost offsets that are greater than or equal to the drug costs. Managed care's goal should be to optimize care and outcomes in a way that minimizes the cost of treating the rare condition. Managed care also should keep in mind that the model of care for hemophilia, as described below, can be a model of care for many other congenital diseases with costly treatments, such as those treated with enzyme-replacement therapies.

HEMOPHILIA

Hemophilia is an X-linked recessive bleeding disorder that affects approximately 1 of 5000 live male births.¹ Currently in the United States, approximately 400 to 500 babies are born with hemophilia each year, and there are a total of approximately 30,000 affected individuals. Males are almost exclusively affected, yet females who carry the genetic mutation may be symptomatic, depending on the clotting factor level.²

Hemophilia A, characterized by decreased activity and/or levels of Factor VIII, affects 80% to 85% of hemophilia patients. Hemophilia B, characterized by decreased activity or levels of Factor IX, affects 15% to 20% of hemophilia patients.²

As shown in the **Table**, most hemophilia patients are classified as having severe disease and have levels of Factor VIII or IX of less than 1%. They experience approximately 2 to 4 bleeding episodes per month, many of which are spontaneous (ie, there is no apparent inciting cause). The remaining affected patients have a less severe form of the disease, with Factor VIII or IX activity levels between 1% and 40%.

Hemarthrosis: A Common Complication of Hemophilia

Patients with severe hemophilia frequently experience spontaneous intra-articular hemorrhages, mainly in the ankles, knees, and elbows. Over the long term, repeated episodes of hemarthrosis may cause irreversible damage to the joint, leading to hemophilic arthropathy, which is characterized by joint stiffness, chronic pain, and a severely limited range of motion.³

In a longitudinal 6-year study performed during the 1980s and 1990s, 90% of people with severe hemophilia experienced chronic degenerative changes in 1 to 6 joints by the age of 25 years.⁴ In another study, 42% of patients with severe hemophilia were restricted in their physical activities because of arthropathy.⁵

Table. Profile of Hemophilia^a

Classification by Disease Severity	Severe (50%-70%)	Moderate (~10%)	Mild (30%-40%)
FVIII/IX activity	<1%	1%-5%	>5%-30%
Frequency of bleeding episodes	~2-4/month	~4-6/year	Uncommon
Cause of bleeding episodes	Majority spontaneous	Minor injury	Trauma, surgical intervention

^aReprinted with permission from Schmaier AH, Thornburg CD, Pipe SW. Coagulation and fibrinolysis. In: McPherson RA, Pincus MR, eds. *Henry's Clinical Diagnosis and Management by Laboratory Methods*. 21st ed. Philadelphia, PA: Saunders Elsevier; 2006:729-746.

A critical factor for avoiding the occurrence of hemophilic arthropathy is the prevention of articular hemorrhages.³ However, despite regular infusions of antihemophilic concentrate at an early age, recurrent joint bleeding and the possibility of hemophilic arthropathy still persist in some patients.⁶ Innovative strategies for the prevention and treatment of this common and serious complication are therefore required.

Several treatment regimens are utilized for the care of patients with hemophilia. One regimen, on-demand therapy, is defined as the administration of clotting factor concentrates at the time of an acute bleed. Another regimen, prophylaxis, consists of the administration of clotting factor concentrate in advance of active bleeding with the intention of preventing bleeding events and associated subsequent damage to the affected area. Prophylaxis can be primary (ie, prevention of bleeding events starting early in childhood before the development of a hemarthrosis) or secondary (ie, prevention of bleeding events in those patients with a history of previous bleeding events). Prophylaxis has been documented to improve the joint health and quality of life for many patients with severe hemophilia. Pain also may be averted or mitigated by prophylaxis strategies.⁷

Available data demonstrate that prevention of bleeding episodes from an early age enables hemophilia patients to avoid or reduce the clinical impact of joint disease and improve psychosocial development and quality of life.⁸ For example, young patients on prophylaxis are better able to participate in physical activities, regularly attend school, and achieve their academic and personal goals.

Hemophilia and Inhibitors

One of the most serious and costly complications of hemophilia is inhibitor formation.⁹ As many as 20% to 30% of severe hemophilia A patients¹⁰ and approximately 1.5% to 3% of those with severe hemophilia B¹¹ develop a neutralizing antibody—called an alloantibody inhibitor—directed against the exogenously administered factor replacement therapy required to treat or prevent bleeding episodes. Most inhibitors develop early in life at a median age of 1.7

to 3.3 years and after a median of ~9 exposure days (ie, the number of days the patient was exposed to any clotting factor replacement therapy).¹²

When inhibitors develop, the administration of normal replacement therapy to achieve hemostasis may fail, requiring the use of “bypassing therapies.” For patients with high titer inhibitors, examples of bypassing therapies include rFVIIa and an activated prothrombin complex concentrate. When inhibitors develop, there is a decreased ability to perform needed or elective surgery and an associated increase in morbidity and mortality.¹³

While hemophilia patients with inhibitors comprise a minority of an HTC’s patient population, they often require many times the hours of care and volume of services utilized by their counterparts without inhibitors. Patients with inhibitors require intensive treatment interventions with frequent telephone interaction, education, emotional support, and appropriate plans for pain management.

The total cost of care for patients with alloantibody inhibitors is much greater than that for patients without inhibitors. In addition to requiring more costly therapies, hemophilia patients with inhibitors are often hospitalized at a higher rate. Also, hospitalizations for inhibitor patients may be more prolonged or complicated.¹⁴

Regardless of the severity of disease and presence of inhibitors, the treatment of hemophilia is complex and requires expert evaluation and knowledge of the disease and individual patient. Therapies are costly and dosing varies from patient to patient. An experienced physician’s medical direction is required for appropriate care.

HEMOPHILIA TREATMENT CENTERS

Hemophilia treatment centers have demonstrated their ability to deliver high-quality, cost-effective care for patients with hemophilia. Patients who received care directly from, or coordinated through, an HTC experienced a 40% reduction in mortality.¹⁵ Patients treated as part of an HTC program experienced better outcomes than patients cared for outside of the HTC network, even though the population treated within an HTC is composed of a higher percentage of patients with severe disease and those with blood-borne viral infections and/or inhibitors. Also, patients treated within the HTC network experienced a significant reduction in bleeding-related hospitalizations, especially those on home therapy, compared with patients without an HTC relationship.¹⁵

As of January 2011, there were 141 federally funded HTC across the country.^{16,17} (The HTCs are partially funded by federal support from the Health Resources and Services Administration [HRSA] and the Centers for Disease Control and Prevention. As of 2009, government funding for HTCs was approximately \$11 million.) Hemophilia treatment centers are a model of comprehensive care for a chronic, rare disease. As such, HTCs provide multidisciplinary programs including direct medical care, patient support, patient education, genetic and mental health counseling, and physical therapy. In addition, HTCs may offer an integrated pharmacy program. Through this coordinated approach to care, HTCs are able to cost-effectively accomplish their primary goal of achieving optimal patient outcomes.

Direct Medical Care

Each HTC has a core team of providers that includes hematologists, nurses, social workers, and physical therapists. Patients and their families are integrated into and considered key members of the care team. The HTC coordinates care of its patients across a variety of medical disciplines and specialties, including but not limited to primary care, orthopedics, genetics, pharmacy, dentistry, and educational/vocational counseling.

Providers at HTCs evaluate most individuals with severe hemophilia at least annually. The frequency of visits may depend on age, therapeutic regimen of care, and associated morbidities or conditions. The number of visits also depends on the patient's geographic access to the HTC or an HTC-based outreach program.

For each patient, the HTC team determines the optimum care regimen, which may range from primary prophylaxis to secondary prophylaxis to on-demand therapy. The regimen is based on each patient's diagnosis and associated clinical course. In addition, HTC team members are experts in the management of bleeding events and are critical for the planning of elective diagnostic or therapeutic invasive procedures.

Clinical/Patient Support Programs

Hemophilia treatment centers provide many important services in addition to direct medical care. These include, but are not limited to, patient/family education, research, outreach, emotional support, and oversight of home care services. HTC team members are available by phone 24 hours per day, 7 days per week, for intervention and consultation. HTCs provide these services to enhance the quality of their patients' lives, improve outcomes, and decrease disease-associated morbidity and mortality.

The HTC staff also develops annual care plans for those patients who are located miles away from the HTC and who may receive their daily and routine care from their local hematologists or other medical care providers. The medical community frequently considers the hematologists within the HTC to be the local and regional experts in bleeding and clotting disorders. The HTC hematologists also provide the specialized laboratory expertise necessary to diagnose these rare bleeding and clotting disorders in a timely and accurate manner.

Physicians and nurses at HTCs teach patients and their families how to quickly and effectively manage bleeding episodes in the home and when to contact the HTC for advice and intervention. Also, HTC staff may educate primary care and hospital providers, dentists and other specialists, schools, and employers about hemophilia. Many of the people and organizations involved in a hemophilia patient's life do not completely understand the disease, or have misconceptions. The HTC staff ensures that these groups understand the patient's disorder, the need for safety measures and emergency protocols, and the treatment regimen and activity restrictions for individual patients.

Pharmacy Program

Many HTCs have an integrated pharmacy program, which offers access to therapy and allows close medical involvement for bleeding events. More than half of the HTCs are qualified entities under HRSA's 340B Drug Pricing Program. Section 340B limits the cost of covered outpatient drugs to certain federal grantees (including HTCs), federally qualified health center look-alikes, and qualified disproportionate-share hospitals.¹⁸ The main purpose of the 340B program is to stretch federal resources provided for hemophilia care as far as possible, thereby reaching more eligible patients.¹⁹ As 340B entities, HTCs realize significant savings on the cost of factor products.¹⁸

Hemophilia is a rare disease with a well-established network of comprehensive centers of excellence and expertise. Translation of advances in hemophilia care is carried out in these centers of excellence in a cost-effective fashion, and these efforts have led to improved survival and quality of life. The ability to maintain, advance, and promote excellent care for individuals with hemophilia and other rare bleeding disorders depends on the preservation of the HTC network despite the present environment of reduced federal funding support and truncated reimbursement for time-intensive comprehensive care. The federal government has enabled HTCs to survive through purchasing and selling replacement therapy products through the 340B mechanism while providing

the important benefit of passing along a reduced cost of replacement therapies to participating patients.

In summary, through state-of-the-art medical care and comprehensive support in addition to integrated pharmacy programs, the HTC team strives to decrease morbidity and mortality and decrease costs, such as those associated with unnecessary emergency department visits or inappropriate use of expensive replacement therapy.

HEMOPHILIA AND MANAGED CARE

Hemophilia is a chronic condition that affects a limited population. Therefore, health plans may not devote as much attention to the management of hemophilia as they do to more prevalent diseases with a greater budgetary impact.

Current medical and pharmacy policies related to hemophilia often are limited to prior authorization or pre-certification for clotting factor replacement therapy. The primary goal is to ensure that products and technologies are used within labeling and according to best clinical practices. A secondary objective can be to identify hemophilia patients who experience a significant bleeding event requiring hospitalization and costly therapy management. For these patients, health plans may make case management services available to minimize barriers to care and improve its quality.

Given the complexity and cost of care for individual hemophilia patients, there may be opportunities for health plans to play a more active and effective role in managing these disorders.

To successfully improve a health plan's approach to hemophilia, pharmacy & therapeutics (P&T) committees might seek to address the issues described below. Once these issues have been considered for hemophilia, there may be an opportunity for health plans to apply their experience and insights to other chronic, rare diseases that have a significant per-patient cost.

Education Within the Health Plan

As reflected by webinar participants, many pharmacy and medical directors and case managers are not familiar with the complexities of hemophilia care and the HTCs' approach to improving the quality of care while managing costs. Many of these health plan executives said they would benefit from education addressing the following topics: (1) a better understanding of hemophilia treatment and potential complications associated with hemophilia, (2) approaches for improving outcomes, (3) the nature and benefit of prophylaxis, (4) the nature of inhibitors and how they are managed, (5) genetic counseling, (6)

management of pregnancies and deliveries of hemophilia carriers, and (7) new hemophilia therapies in the pipeline.

Education on these topics would help payers implement policies that foster improved quality of care. For example, education about prophylaxis and its benefits could help payers better understand the value of a significant near-term investment that could yield long-term benefits. A better understanding of inhibitors and the associated cost of care might encourage health plans to more closely monitor these hemophilia patients and encourage them to seek care from HTCs.

Partnering Between Health Plans and HTCs: A Key Activity

In 1954, NHF formed a Medical and Scientific Advisory Council (MASAC) to advance clinical care and promote hemophilia research. This council establishes quality-of-care guidelines for the treatment of hemophilia and other bleeding disorders. Issued in the form of recommendations, MASAC guidelines set the standard of care for HTCs and other providers around the world. The guidelines are referred to by an international array of physicians, medical schools, pharmacists, emergency department personnel, insurance companies, and others.²⁰ The scientists, physicians, and other treatment professionals who comprise MASAC are internationally regarded as experts in the broad field of bleeding disorders research and care, AIDS, hepatitis, other infectious diseases, and blood safety.²⁰

All MASAC guidelines are published on the NHF Web site.²¹ MASAC has published 77 guidelines covering such topics as standards of care (MASAC #132), prophylaxis (MASAC #179), and preferred drug lists (MASAC #166). HTCs and specialty pharmacies that provide care for hemophilia patients are encouraged to comply with these guidelines.

Given the quality of care HTCs provide based on MASAC guidelines, there are opportunities for health plans and HTCs to partner more effectively. For example, HTC-based providers offer expertise that could assist health plans with the development of evidence-based policies and guidelines for hemophilia management.

Health plans' case managers coordinate care and provide support for patients with a range of morbidities. As previously described, HTCs also coordinate care and provide support for hemophilia patients. Therefore, a closer working relationship between the health plans and HTCs could enhance care and limit duplication of effort. One option is for the HTC to act as the lead medical manager for a health plan's hemophilia patients. Health plans could directly or through other available resources provide case management services for members without access to HTCs

while encouraging these patients to connect to the HTC network.

Webinar participants were generally unaware of HTC efforts to manage the cost of care. For example, HTCs typically do not authorize automatic medication refills or auto-shipment of expensive pharmaceuticals. HTCs work with patients to verify the number of bleeding episodes and the quantity of medications administered since the previous refill. HTCs closely monitor for appropriate dosing. HTCs are cognizant of cost issues and proactively manage them. Working more closely together could enable payers and HTCs to identify new avenues to better manage costs while enhancing the quality of care.

One of the challenges that health plans might encounter in developing a closer relationship with HTCs is that a provider contract might not yet be in place. Health plans may have contracts with some HTCs and not with others. Webinar participants suggested that health plans assess the potential for formal relationships with all HTCs within the payer's membership area.

When contracting with HTCs, health plans can contract for medical services or for both medical and pharmacy services. When selecting a source for factor products, webinar participants suggested that health plans consider the acquisition cost of the drug, the availability of education aimed at teaching hemophilia patients about appropriate administration, and the degree to which the pharmacy monitors the dispensing, administration, and utilization of factor products.

Health plans could mandate and cover the cost of annual evaluations of hemophilia patients in the HTCs to fine-tune their treatment plans for replacement therapy, HIV and hepatitis C virus care, physical therapy regimens, and so forth prior to renewing their 340B clotting factor prescriptions. This approach would achieve the mutual objective of delivering cost-effective care within the context of the highest standard of care.

Another challenge potentially facing health plans is that their knowledge of hemophilia and their relationships with HTCs are spread over many people, each of whom may have limited knowledge of the disease. This approach can hinder development of a uniform and effective relationship with the HTCs. P&T committees should evaluate the benefit of developing a centralized and stable group of medical directors, pharmacists, and case managers who are current HTC participants responsible for managing hemophilia patients. This group would be able to interpret, scrutinize, and evaluate the appropriateness of adopting or adapting the recommendations generated by MASAC. An integrated approach to patient care planning involving both the health plan and the HTC team could act as a focal point throughout

the health plan's service area. The HTCs would know who at the health plan to contact on behalf of their patients. Both the health plan and HTCs would develop a better understanding of how to work together more effectively.

Relationships Between Health Plans and Specialty Pharmacies for Hemophilia Patients

Health plans may opt to work with specialty pharmacies to deliver coagulation replacement products for the plan's members with hemophilia, especially when those members do not have access to an HTC or choose not to go to an HTC. The NHF's MASAC has developed a set of standards of service for providers of clotting factor in the home. The guideline is identified as MASAC #188.²²

Among its requirements, MASAC #188 recommends that specialty pharmacies offer clinical expertise and experience in hemophilia, deliver medications within 48 hours on a routine basis and within 3 hours (if logistically possible) for emergencies, fill all prescriptions within $\pm 5\%$ to 10% of prescribed assays, carefully manage clotting factors based on expiration date, and provide 24/7 availability in multiple languages.²²

The NHF lists on its Web site those HTC pharmacy programs, specialty pharmacies, and home care providers that are known to comply with MASAC #188.²¹ (For more information about MASAC #188 and other MASAC recommendations, please visit the NHF Web site at www.hemophilia.org.) Webinar attendees suggested that payers select among the HTCs, specialty pharmacies, and home care providers in compliance with MASAC #188 based on (1) the cost of the factor products, (2) the breadth and quality of support services, (3) the efficiency and effectiveness with which the services are delivered, and (4) the agency's relationship with the patient. Webinar attendees also suggested that health plans consider encouraging specialty pharmacies and home care providers not on the list to examine and adhere to MASAC #188 standards.

Encouraging Care Consistent With Best Clinical Practices

Encouraging care consistent with best clinical practices means basing a health plan's policies on the results of clinical trials, evidence-based guidelines, and published literature. Webinar attendees suggested that one way to accomplish this goal is to explore and adopt, to the fullest extent possible, the practice guidelines developed by the NHF's MASAC. In those areas where evidence-based data are not available, HTCs and health plans could develop clinical research projects intended to generate the data.

Webinar attendees suggested that another strategy is for P&T committees to ensure that the health plan's policies provide incentives for patients to receive routine care outside of an emergency department. For example, copays and deductibles should support access to routine care at an HTC or physician's office and encourage therapy compliance.

Webinar attendees also suggested that health plans consider using prior authorizations to ensure that medications are delivered in compliance with MASAC #188 or to identify hemophilia members appropriate for case management programs who do not have access to an HTC or do not want to use an HTC. The objective is to design prior authorization requirements that encourage high-quality care for hemophilia patients.

Webinar attendees suggested that health plans and HTCs can work together to develop evidence-based prior authorization requirements that maximize patient benefit while limiting cost to the health plan and minimizing any potential for a delay in the delivery of care.

Investing in Care Today to Improve Long-Term Clinical Outcomes and Achieve Cost Savings

Most webinar attendees reported that their health plans support prophylaxis as the standard of care for severe hemophilia. These payers realize the quality-of-life and economic value of prevention or delay in progression of joint damage. Health plans should evaluate their policies to determine the appropriateness of encouraging prophylaxis and, if appropriate, how best to support it as the standard of care for severe hemophilia.

Webinar attendees noted that many health plans invest in prophylaxis even though hemophilia patients may change plans before the individual benefits of prophylaxis are realized. The webinar attendees believed that prophylaxis contributes to their health plan's mission of delivering high-quality care, even if the long-term benefits are not evident during the period of coverage. More research is warranted into the appropriate age for patients to start and stop primary prophylactic regimens and the range of clinical and economic benefits realized from these regimens.

Webinar attendees suggested that healthcare reform could affect their approach to prophylaxis. For example, if the removal of lifetime benefit caps remains in place, fewer hemophilia patients might change their health plan and those that do change might do so less frequently. Removal of lifetime benefit caps could result in a rise in the number of hemophilia patients able to receive prophylaxis. Many webinar attendees suggested that P&T committees should reexamine hemophilia-related issues

as the nature of healthcare reform evolves and becomes clearer.

Potential Impact of Cost Sharing on Patient Compliance and Persistence

As the cost of healthcare rises, many employers and payers seek greater cost sharing from patients. Due to their high cost of care, many hemophilia patients currently struggle to meet their financial responsibilities. Webinar attendees suggested that health plans and HTCs work together to address these barriers to care, as they may impact therapy compliance. For example, health plans can work with HTCs to ensure that their hemophilia patients are using in-network providers and that underinsured patients are applying for patient assistance programs, as available.

CONCLUSIONS

Hemophilia is an example of a chronic, rare disorder associated with a significant cost per patient. While rare diseases often do not generate significant attention in many health plans, there are opportunities to optimize care as well as more effectively manage costs. Health plans that access the opportunities available through HTCs for better managing hemophilia patients are likely to develop strategies that deliver a positive return on investment. Creative cooperation between health plans and HTCs is likely to better serve mutual patient constituencies. It also is possible that some of the strategies health plans implement for their hemophilia members can be appropriately applied to other chronic, rare diseases with a high per-patient cost.

For further information about hemophilia and MASAC guidelines, please refer to the NHF Web site at www.hemophilia.org. The slides for the 6 webinars that formed the foundation for this article are posted on the NHF Web site as well as the Web site of the Pharmacy & Therapeutics Society (www.pandtsociety.org).

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