Clinical Updates in Hemophilia Managed Care and Specialty Pharmacy to Improve Cost-effective and Comprehensive Care

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Introduction

Hemophilia represents a rare and complex disease state requiring expert care and collaborative management to achieve optimal outcomes. Despite an incidence of only 1 in every 5,000 live male births, this lifelong bleeding disorder commands a disproportionate share of health care resource utilization, with medical claims costs in excess of 20 times higher than the average commercial plan member. The inherently intricate treatment of hemophilia is further complicated by challenges related to care via an array of medical specialties and sequela arising from chronic, often spontaneous, bleeding episodes. The development of inhibitors, characterized by antibodies to clotting factor concentrate, affects approximately 15% to 20% of patients with hemophilia (~30% in hemophilia A vs 2%-5% in hemophilia B) and is by and large the most significant and costly complication associated with the disease, pushing average per patient costs beyond $700,000 annually.

Recognizing the substantial clinical and economic burden associated with hemophilia—including the highly specialized care required for those patients with inhibitors to clotting factor concentrate—a network of hemophilia treatment centers (HTCs) was formed more than 40 years ago. Since their inception, HTCs have served as the preeminent centers of excellence in hemophilia care, featuring a multidisciplinary team with expertise in the management of patients with bleeding disorders. HTC care is associated with improved outcomes in the management of hemophilia, including reduced mortality and hospitalization rates. A CDC-sponsored study of 3,000 individuals with hemophilia showed that those who received care in an HTC had a 70% lower mortality rate and a 40% lower hospitalization rate compared with those who received care in other settings.
In addition to payers and HTCs, the other integral stakeholders in hemophilia management are specialty pharmacy providers (SPPs). SPPs are often contracted by payers to distribute medications and provide support services for patients with hemophilia, either independently or in conjunction with an HTC. Hemophilia specialty pharmacy programs often employ disease or case management services to facilitate therapeutic adherence through patient education and on-call nursing or pharmacy support. In addition, SPPs manage factor assays, ensuring that the prescribed clotting factor concentrate, in the correct dosage, is delivered when and where the patient needs it. Assay management is essential to minimize the over-utilization of factor products and control costs.

Acknowledging the multiple groups of stakeholders necessary to provide seamless, value-based care for individuals with hemophilia, recent efforts sponsored by the National Hemophilia Foundation (NHF) have centered on collaboration and open dialogue among HTC, payer, and specialty pharmacy thought leaders. Consensus meetings of the NHF’s Comprehensive Care Sustainability Collaborative (CCSC) have brought together HTC and payer representatives for the purpose of developing a hemophilia quality improvement (QI) initiative across the nation, while supporting HTC sustainability and the comprehensive care model. Further NHF-sponsored programs have built upon this momentum, bringing HTC, specialty pharmacy, and payer stakeholders together in a forum promoting open, collaborative dialogue.

In keeping with this theme, an expert panel discussion assembled to discuss interventions to overcome current clinical challenges in the management of hemophilia as well as opportunities to streamline payer, provider, and specialty pharmacy interactions to that end. Also discussed was the future of hemophilia care and the potential impact of novel agents expected to enter the therapeutic space in the near future. Interactive, case-based dialogue was employed to gain insights on particular patient scenarios from the perspective of HTC, payer, and specialty pharmacy leadership. Comprising the expert roundtable were:

Jonathan Roberts, MD  
Hematologist  
Assistant Research Director  
Bleeding & Clotting Disorders Institute

Celynda G. Tadlock, PharmD, MBA  
Vice President, Pharmacy Business Development  
Aetna

Michael Zeglinski, RPh  
Senior Vice President, Specialty Pharmacy  
OptumRx®/BriovaRx®
Expert Panel Discussion

What are the greatest management challenges for hemophilia in the inpatient and clinic settings? Please characterize the most prominent clinical challenges in terms of comorbidities, disease severity, and complications.

JONATHAN ROBERTS, MD: In the inpatient setting, even at our hospital where we already manage a number of these patients, it can be a challenge getting hospital staff to feel comfortable managing patients with severe bleeding disorders, like hemophilia. Because of this, we administer a tremendous amount of provider education in the hospital setting for pharmacy professionals, nursing staff, residents, and other specialties. This is a patient population with a rare condition, so making sure that the hospital staff feels comfortable taking care of our patients is one of the greatest inpatient challenges.

... IT CAN BE A CHALLENGE GETTING HOSPITAL STAFF TO FEEL COMFORTABLE MANAGING PATIENTS WITH SEVERE BLEEDING DISORDERS ...

In the outpatient setting, one of the greatest challenges is negotiating with insurance companies to meet criteria of prior authorizations necessary to get our patients the care they need. The ultimate goal of these interactions is to have the insurance companies understand that we’re experts in treating patients with bleeding disorders. Sometimes we have to jump through many “hoops” to get certain clotting factor products covered or to transition a patient to an extended half-life (EHL) product when there’s higher costs involved; providing clinical justification to payers for necessary therapies is a time-consuming challenge.

In terms of comorbidities, thankfully the treatments for HIV and hepatitis C have improved dramatically over the past few years. For our patients with hepatitis C who have perhaps waited more than a decade for treatment, there are now therapies with near 100% cure rates and minimal side effects. As a result, we’re finding that we’re treating our patients with hepatitis C successfully, making that particular comorbidity less challenging than it was in the past. Additionally, patients with HIV infections also have much better therapies available now, and we’re having great success managing those individuals with hepatitis C and HIV. However, I think as the paradigm has shifted to a virtual 0% risk of viral transmission from our new recombinant and EHL products, hepatitis C and HIV are thankfully becoming more manageable and a thing of the past in patients with bleeding disorders.
As far as complications with inhibitors, I think the biggest challenge is facilitating patient adherence to immune tolerance induction (ITI) therapy and, to a certain extent, making sure that the managed care organizations are on board with such a high-cost intervention. ITI can be upwards of 60% to 80% effective in eradicating inhibitors, but it can also take years. Achieving that necessary approval or buy-in from payers has been an ongoing issue in providing care for patients with inhibitors.

CELYNDA G. TADLOCK, PHARMD, MBA: From a payer perspective, it’s certainly very complex when you look at the clinical challenges, and I can only imagine those challenges are amplified for prescribers who also have to work with many different large national, regional and local insurance companies. Many of those challenges are due to the stages of precertification that have been designed around more of a generalist model. In this model, we have generalist physician medical directors that are highly trained but are also dealing with more than 500 different diagnostics, procedures, and surgeries, not to mention the innumerable pharmacotherapies prescribed by network providers on a given day. As a result, we’re seeing an evolution across our company to incorporate centers of excellence. For hemophilia, we have our National Medical Excellence Program that collaborates with the HTCs and those experts are then tied into experts in other large disease states, such as HIV and hepatitis C. This coordinated, quality-driven infrastructure culminates in three highly specialized units collaborating with each other.

As we move away from this generalist approach to more of a specialist approach, someone that is primarily dealing with hemophilia case review links up with someone that may be the regional expert in the case review process for HIV and hepatitis C. We’ve established a developing network of connectivity that is extremely important to manage these patients so that we can better coordinate the end review process. Eliminating the generalist approach results in these cases being looked at more holistically from the payer perspective, by experts that intimately understand hemophilia and the comorbidities associated with it. We know—at least from our experience with hemophilia and certainly the initial data from...
last year alone with hepatitis C—that we avoided a lot of expenditures and experienced a high rate of prescriber agreement relative to coverage determinations. Approximately $35 million in avoided expenditures were achieved by patients being treated with high-quality formulary products versus the originally prescribed product for hepatitis C.

JONATHAN ROBERTS, MD: That’s why we have people at our HTC dedicated to navigating prior authorization with insurance companies to ensure those vital high-cost therapies are covered. However, I think because we’re an HTC, already designated as a center of excellence, we’ve had pretty good luck getting different therapies covered for our patients that need hepatitis C and HIV treatment.

Conversely, we do get asked by insurance companies for justification on why we need to treat. For example, if a patient with hemophilia goes untreated for hepatitis C and as a result develops chronic cirrhosis, there is a good chance that patient with go onto end-stage liver disease. And obviously performing a liver transplant in a person with a severe bleeding disorder is no small undertaking and can be extremely expensive; that patient will cost multiple hundreds of thousands, if not more, for factor products, sometimes dealing with postoperative morbidities, prolonged hospitalization, and complications. Taking these potential outcomes into consideration, I think it’s good that payers are looking at the benefits of spending $100,000 for a hepatitis C treatment that’s exceedingly efficacious and tolerable as a means of avoiding the long-term morbidity of future hospitalization, liver transplant, and immunosuppressive therapies. These complications can be a lot more costly in the long term than current new therapies for hepatitis C.
Can you briefly explain how HTCs are uniquely positioned to meet the clinical challenges we just discussed and optimize outcomes in hemophilia via the comprehensive care model? How do you see the role of HTCs changing in the future with the advent of new therapies?

JONATHAN ROBERTS, MD: HTCs serve as the medical home for patients with bleeding disorders. They see us as their specialists as well as their primary care providers, and we really do a lot of care coordination among all of the other subspecialists that the patients may need. We have physicians, advance practice nurses (APNs), pharmacists, nurses, and other staff members that are dedicated only to patients with bleeding and clotting disorders. Furthermore, we are active in collaborative research across the country and are helping produce treatment guidelines that are shaping the field. When we collaborate with other HTCs, it truly creates a national and international network of support for people with bleeding disorders. In this capacity, HTCs are genuinely important because they offer unparalleled expertise in rare bleeding disorders with tremendous ancillary staff to support their efforts. We are uniquely positioned experts for these patients and managed care organizations pay attention to that.

The ongoing Comprehensive Care Sustainability Collaborative (CCSC) meetings recently brought to light a few papers published in the past that show the value offered by HTCs in terms of disease outcomes. Patients that are treated outside of HTCs have a 1.7 relative risk of increased mortality and a 1.4 relative risk of increased hospitalizations compared with those treated within HTCs.5,6

For patients receiving care outside of an HTC: Mortality rate increases by 70% and hospitalization rate rises by 40%

![Graph showing relative mortality and hospitalization rates for HTC vs. other sources of care.](image-url)
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Studies such as those offer objective evidence demonstrating that we help patients achieve better outcomes, that we reduce their mortality, and that we keep them out of the hospital. And those are just a few, small objective pieces of data showing how we provide optimal management of individuals with hemophilia and other bleeding disorders.

In the next five years I think we’re going to see even more EHL products and even newer biologic therapies that will offer multiple treatment options for individuals with hemophilia. Right now, we’re in an age where we have plasma-derived products, we have recombinant factor VIII products, and then we have EHL products. However, there are some investigational biologics that are potentially going to provide subcutaneous, once-weekly—or even less frequent—dosing. In addition, we’re moving towards truly effective gene therapies for patients with hemophilia B and, soon, patients with hemophilia A.

As a result, I think the next five years are going to bring about a treatment paradigm shift, where as researchers and as clinicians we’re really going to have to work towards finding the right treatment strategies to tailor therapy to an individual patient’s needs. I think there are going to be a lot of options out there and I don’t think there’s going to be any “one-size-fits-all” approach for treating patients. It’s really going to be an exciting time and we’re going to have to ask a lot of good research questions to do the appropriate studies and look at whom these specific therapies are best suited. So I think there’s going to be a big push towards individualization of therapy and that’s going to have to be looked at from the perspective of clinical efficacy, as well as the cost of these new therapies. Those are things that we don’t know yet, so I think we’re going to have to be vigilant about making the right treatment decisions from a lot of different aspects of the patient’s life.
Can you offer your insights on the role that specialty pharmacy providers (SPPs) share in the management of patients with hemophilia? Please briefly describe some of the specialized tools and technology platforms you have at your disposal to actively monitor and manage these patients.

MICHAEL ZEGLINSKI, RPH: From my perspective, having been in the specialty pharmacy business for over 20 years, I’ve had some great experiences working with HTCs and the physicians, nurses, and care teams at the centers. I’ve seen the positive impact that the treatment centers have had. And I’ve also seen a change over the past 20 years in how pharmacies have helped support the treatment centers and patients. It goes beyond the standpoint of simply dispensing factor product, which is the role that most people see a pharmacy as having. It extends to keeping adequate inventory and having pharmacists and nurses that understand the disease state, comorbidities, and unique needs of the patients. In this manner, specialty pharmacies provide counseling to augment what the treatment center is doing.

Specialty pharmacies are charged with working through all the issues of getting product to patients when they need it, especially if they have unexpected bleeds and they’re outside of prophylactic regimens.

What I’ve seen is that the expectation of specialty pharmacies has certainly changed from being a product-centric pharmacy, that is mainly just getting the product there, to looking at all sorts of other areas where they can provide support. We look at product distribution, nursing support, providing home-based nursing, teaching people to self-infuse, and supporting them if they’re unable to infuse or their caregivers are unable to infuse. In addition, especially as the cost of the products has increased and insurance has played a prominent role, we make sure that people can get their treatment covered by assay management. Assuring that, based upon what the prescribers are ordering, we’re getting as close as possible to that ideal dose to minimize any wastage. There are a lot of products that have come onto the market in the past 20 years, the assay ranges are much broader, and the pharmacies are able to do a better job of getting much closer to the true prescribed dose, thereby minimizing wastage.

In addition, technology has really come into play as patients use smart phones and tablets and have increased access to the internet and more information on their own. Where they might have been looking at the
treatment centers, healthcare professionals, or the pharmacies as their source of information in the past, now there’s a broad base of information available to people through NHF, publications on the web, chat rooms and blogs, and other patients merely sharing their experiences. On the specialty pharmacy side, what we’ve seen as being effective and supportive is looking at how to interact and assist in care in different ways by using technology.

One of the ways that we’ve been successful in harnessing that technology is by using a form of media that is common to all: video consults. Although many of us use FaceTime or Skype for conversations with family and friends, we haven’t seen that come into widespread use by other specialty pharmacies. We’ve been able to implement this technology by allowing our pharmacists and nurses to actually have face-to-face conversations with patients via video to assist them along their treatment journey. If a patient has a problem and we can’t be there to see it, we’re able to actually look at what’s going on via video and assist them in that way.

There are also apps out there to log infusions, categorize the location of bleeds, and create a longitudinal path of information that can be reviewed by physicians, nurses, and pharmacists. There’s much more that we’ll be able to do in the future with smart phone technology that I think specialty pharmacies are going to have to really look at and use creatively.

**JONATHAN ROBERTS, MD:** I think the technology I’ve seen used the most are the smart phone apps, and there are offerings from multiple vendors that each have their own advantages and disadvantages. One of the ways that these apps can really help is in patients logging their bleeds and making the whole process less cumbersome. We still have people who use paper bleed journals where they record their lot number, the location of the bleed, or if it was a prophylactic infusion, but those tend to be cumbersome for the patients. At nearly every comprehensive care visit, I talk with my patients about the new apps that are available. For example, we encourage our patients to be involved in the American Thrombosis and Hemostasis Network (ATHN), which is a collaborative database that’s used for many different research studies and data gathering. They have an app called ATHNadvoy that allows patients to quickly and easily log the details of their infusion
in under a minute, and—if there is a bleed—they can document the area of the bleed, the severity, and log other details. Then the pharmacy, nurses, APNs, and physicians at our HTC all have access to that data. So we don’t necessarily have to wait for the patients’ biannual or annual comprehensive visit to go over bleeds that they’re having. We can notice bleed trends more readily and can be a little bit more assured that the integrity of the data is there. Because they’re logging bleeds in real time, we’re not worried about the patients sitting in the parking lot prior to their visit and filling out all of their infusion logs to their best recollection of how many bleeds they’ve had in the past six months. Some patients actually do that, and obviously it’s inaccurate.

We haven’t really explored FaceTime or video conferencing capabilities at this point. However, because we have quite a large referral area, we’ve looked at some telemedicine options. In the next five years or so, I think telemedicine is going to be increasingly integrated into the HTC model.

**Patients may even be able to monitor their factor levels based on past pharmacokinetics and based on their last infusion.**

More advanced apps are forthcoming. Patients may even be able to monitor their factor levels based on past pharmacokinetics and based on their last infusion. There’s a lot more information available and I think we just have to figure out how to integrate that into our patients’ lives. Of course there is a bit of a time lag with patients being receptive to change too. So I think it’s going to take a little time, but there are some exciting things coming.
Please characterize the most prominent, current challenges in terms of home care and patient engagement. What do you see as being potential future challenges in these areas?

MICHAEL ZEGLINSKI, RPH: Some of the current challenges that we have regarding home care and patient engagement have been in place for 20 years. Namely, how do we look at patients as individuals and deal with them and their own unique needs differently? You can’t look at one person with hemophilia and treat them the same way you treat a different patient. The reason, obviously, is that there are so many different facets to what’s going on in a particular patient’s life. The patient’s age, disease severity, home life, and financial situation, including insurance coverage, all need to be looked at on an individual basis. Everyone has their own unique story regarding what they deal with every day. So the current challenges remain the same in that we’re all people; this is a complicated disease to have and it requires a lot of support. From my perspective, considering all the technology that’s available now, people will accept it if they like it and if it’s easy to use. On the other hand, if they’re challenged, if their educational levels are such that they either don’t grasp it or it’s complicated, they won’t use it. Continuing to keep things simple and easy is what I’ve seen as being effective, in addition to rigorous support and just being there for people.

In terms of future challenges from a pharmacy perspective, we have to look at whether we are going to have a different model for providing patients with their products based upon all the new technology coming out. If gene therapy becomes something that is commonplace in future years, how does that change the role of the specialty pharmacy and what support it provides? As new products come to market, as gene therapy comes into the hemophilia space and becomes more commonplace, the role of the specialty pharmacy is definitely going to change.

THE PATIENT’S AGE, DISEASE SEVERITY, HOME LIFE, AND FINANCIAL SITUATION, INCLUDING INSURANCE COVERAGE, ALL NEED TO BE LOOKED AT ON AN INDIVIDUAL BASIS.
From a payer perspective, can you please share your insights regarding these clinical challenges cited by the HTC/SPP panelists? Do these align with your own perception of what the key concerns are for medical and pharmacy providers? What are the key challenges in hemophilia management for payers?

CELYNDA G. TADLOCK, PHARMD, MBA: From a payer perspective, I absolutely agree with those clinical challenges that have been called out in the discussion thus far. What is really key to us is looking at adherence with ITI therapy. As mentioned by Dr. Roberts, tools that can be leveraged to better support patients in adherence are critically important. Dr. Roberts also talked about how it may take years to treat inhibitors at a very high cost. So adherence really becomes an important factor for payers because of the desire to best ensure that patients get the benefit from the investment spent on the treatment and are hopefully able to reduce the amount of time that they would have to undergo ITI.

Going forward, having more products coming to market and more individualized therapies will require us to continue to lean on the HTCs, key opinion leaders in hemophilia, and data from the clinical trials as we start to conduct the P&T committee reviews for all of the EHL products, new biologics, and even gene therapies as they arise. Only by doing so will we be able to make sure that we can continue to provide appropriate therapy that will be highly individualized to the needs of patients.

From a utilization management standpoint, I would say that all of the typical tools such as preferred products and step-therapy are levers that might be deployed with new products coming to market. I don’t see any of those management interventions going away. One of the things that we think about with precertification, quantity limitations, and even site of care optimization is to try to help procure the factor at one of our network specialty pharmacies or through an HTC’s 340B pharmacy program at the best cost. I think what we’re going to see, or what we’re beginning to see now from some of the large national self-insured players, is that they’re more open to most of these management efforts than in the past. Historically, many have been hesitant to embrace to some of the site of care optimization efforts that encourage the use of in-network specialty pharmacies, but now we’re seeing employers ask, “What else can we do?” In the past, they were resistant to have their hemophilia population or others with specific conditions be required to receive product
from a certain location. But now we’re getting the expectation that payers really help in this coordination due to overall rising specialty drug costs.

To that point, I think we’re going to see more coordination around site of care than we’ve seen in the past. I think unfortunately we’ve probably all seen what’s been in the press as it relates to some organizations that may be trying to profit from our hemophilia populations. And because of some of that, I think we’ll also see some increased efforts targeting fraud, waste, and abuse or some increased efforts to further credential the specialty pharmacies that are in our networks. As a result, I think we’re going to see more credentialing efforts; more anti-fraud, -waste, and -abuse efforts; and more site of care steerage that we may not have seen in the past.

JONATHAN ROBERTS, MD: Even if we have to jump through a lot of hoops to get our patients their factor, I think eventually the payers listen. Especially speaking for hemophilia, they’ve listened to our concerns and they’ve listened to us as an HTC center of excellence. So I think the payers are willing. Additionally, there needs to be more guidance and definitely prevention measures for fraud, waste, and abuse of factor products. However, in general, my experience with insurance providers is that they do want what’s best for the patient and that they will listen. As long as we continue to foster a collaborative teamwork mentality among payers, patients, and providers, we will be making strides toward optimizing care for people with bleeding disorders.

Additionally, some manufacturers of factor products have stepped up and provided emergency factor when patients suddenly lose insurance coverage. I think overall the bleeding disorder community as a whole is very supportive, including HTCs, pharmacies, and insurance companies. I think we just need to keep nurturing these collaborative relationships.
Two significant and potentially costly components of hemophilia care—the management of inhibitors and prophylaxis therapy—represent key areas of interest to payers and clinicians alike. Can you describe the current clinical approach in these areas and discuss how emerging therapies such as recombinant factor products and extended half-life agents will affect practice now and/or in the future?

JONATHAN ROBERTS, MD: There are two ends of the spectrum in how clinicians internationally have treated individuals with inhibitors. Specifically, there was a big study that came out a few years ago, the RODIN Trial, that looked at low-dose ITI therapy versus high-dose ITI therapy. Low-dose therapy was defined as 50 U/kg three times a week, and the high-dose group received 200 U/kg daily. Both the high- and low-dose treatment regimens eventually eradicated inhibitors, but in the low-dose treatment group there were more breakthrough bleeds. In my experience, the US approach represents more of a middle ground, where we use 100 U/kg daily, and it’s been efficacious. These studies have used recombinant factor products and plasma-derived products. So really, we don’t have any guidance yet from the literature on how to use EHL products for ITI. These studies are currently ongoing, but the true efficacy and cost-benefit remain largely unanswered. As a result, our practice has not yet moved to EHL products for those patients undergoing treatment for inhibitors.

**The overall take home message for inhibitor eradication** is that patients need to be compliant with their therapy, and they need to work closely with their HTCs. Daily infusions represent a large undertaking to treat patients with inhibitors, and that’s not to mention aspects of prophylaxis or treating bleeds on demand with bypassing agents.
From the payer point of view, how do you evaluate these emerging agents and incorporate them into the plan’s benefit design and existing formulary? In your opinion, is there a general “laissez faire” approach to factor products as potentially life-saving therapies among payers, similar to current strategies with many costly oncology agents, or are you seeing more management initiatives taking hold?

CELYNDA G. TADLOCK, PHARMD, MBA: From a payer perspective, as we look at evaluating these emerging agents, we do some pretty extensive pipeline reporting across all specialty categories including hemophilia. We track what’s on the horizon so that we can keep up with the clinical trials of those emerging agents and get them through our P&T committee process as soon as possible, once available. The agents undergo a typical P&T committee review looking at the safety and efficacy data that are available. In that P&T committee review, we have an expert to represent hemophilia that participates from an outside voting perspective and gives guidance along the way as we prepare the monographs for review.

With specialty drugs getting more and more attention, I think we’re going to see this “laissez faire” approach evolve. We don’t have a preferred formulary for these products right now. We don’t recommend one product over another. Instead, we evaluate these products for their place in therapy and apply utilization management criteria in the precertification process. That could all change years down the road, as we have more and more therapies available in wide supply, or if we have an increasing number of products that might be considered the same or interchangeable, to the extent that there was ever a way to leverage the best price. I think that we can see that happening, but it’s certainly not happening today or in the very near term. As I mentioned before, what I am seeing occur is more of a focus on site of care steerage and pipeline vigilance, engagement with key opinion leaders, and the updating of policies and procedures to better support an individualistic, patient-centered approach.

… A FOCUS ON SITE OF CARE STEERAGE AND PIPELINE VIGILANCE, ENGAGEMENT WITH KEY OPINION LEADERS, AND THE UPDATING OF POLICIES AND PROCEDURES TO BETTER SUPPORT AN INDIVIDUALISTIC, PATIENT-CENTERED APPROACH.
These products can end up being covered under either the medical benefit or the pharmacy benefit, and we make sure that the specialty pharmacy providers in our network are able to bill to the benefit that the patient is covered under. I think the most common benefit that we see them covered under is the pharmacy benefit, but some payers have made the decision to offer them under the medical benefit or both the medical and pharmacy benefit. In response to this variability, we make sure that the dispensers of the factor have the ability to bill any benefit. Then, during the precertification process, they receive guidance as to which benefit to bill.

What collaborative solutions do you envision as providing the most pragmatic opportunities for HTC providers, SPPs, and payer stakeholders to improve outcomes and maintain cost-effectiveness in hemophilia management?

**I THINK INITIATIVES SUCH AS THE CCSC THROUGH THE NHF ARE A GOOD STARTING PLACE WHERE WE JUST HAVE A FORUM TO GET THE DISCUSSION GOING ...**

**JONATHAN ROBERTS, MD:** I think initiatives such as the CCSC through the NHF are a good starting place where we just have a forum to get the discussion going from different aspects in hemophilia care on the national level. Having the CCSC and other initiatives like it is really what needs to happen. We just need to have more open communication, look at the data objectively, and really continue to foster those collaborative relationships.

**CELYNDA G. TADLOCK, PHARMD, MBA:** I touched upon this briefly earlier, but one of the things that we’ve done within our own organization was to set up a National Medical Excellence Program for hemophilia where we employ experts in the disease state. The leadership within that program has a great collaborative relationship with the HTCs. As Dr. Roberts commented, it is critical for providers to be able to access the process of obtaining insurance coverage determinations in a simplified and efficient manner. Especially for this critical condition, it is important for relationships to be established with specialized centers of excellence. The ideal model is not one where it is the first in the queue type of a call center approach; instead, the model should be one where the providers are establishing contacts and relationships with a center of excellence.
We’ve received very positive feedback from the providers relative to our program, and we also believe that there could be some way to get additional input from the members with hemophilia regarding their experience with the program as well. The program is also geared toward patients as they attempt to navigate their out of pocket costs, which despite insurance coverage can be significant, particularly in high-deductible plans at the beginning of the year. There is also a good service available to the members from a financial responsibility perspective that’s being provided by our program.

**MICHAEL ZEGLINSKI, RPH:** From the specialty pharmacy perspective, what really works is when there’s collaboration between the specialty pharmacy, the treatment center, and the payers specific to the marketplace. For example, if you take a particular city in the country and there’s a treatment center and a specialty pharmacy is linked up with that treatment center to provide product, there should be a very close alignment between the two to understand what the treatment protocols and expectations are from both sides. Alignment must also be achieved in terms of how to ideally support each other to provide care for patients with hemophilia. From there, both parties should have a deep understanding of what the payer benefits are in that market. If that city, for instance, has a two-payer system that dominates the market, it’s very important to understand how those products are reimbursed under the plans that those payers offer to ensure that there’s no interruption in therapy due to insurance coverage changes or changes in treatment protocols of which the insurers aren’t aware.

Linking those three groups together has worked very well from my experience in certain marketplaces where there’s true collaboration ultimately focused on ensuring that the patient always has product and that they understand how and when to infuse it. The key stakeholders should be receiving reports to assess whether the treatment protocol is being followed and if there are certain things going on in the patient’s life that require differential treatment from other patients. That’s where I’ve seen the most success and collaboration: when those three groups are all tied together. In addition, building upon what was already said, having true experts within the health plan that understand hemophilia is certainly beneficial for quickly resolving any insurance issues that may come up so that the patients can get the product they need.
Case Study Review and Discussion

Case #1: A 23-year-old Male with Moderate Hemophilia A

- Active patient who enjoys running and playing basketball
- Self-infuses a 1x weekly prophylactic regimen at home
- Required several dosing adjustments to adequately control bleeding due to his...

Is there a trend of treating to a higher trough level, such as 3% or 5%, in active patients such as this one?

What individual patient considerations play into decision making in this particular area?

JONATHAN ROBERTS, MD: The overall goal is to prevent bleeds. If you have a patient on a treatment regimen that’s not working for their lifestyle, then you alter it. The paradigm of keeping a patient’s factor levels above 1% is based on the fact that patients with severe hemophilia will have spontaneous bleeds when their factor levels are less than 1%. Meanwhile, patients with moderate hemophilia and factor levels of 1% to 5% tend to bleed with minor trauma or sometimes with activity, like this gentleman in the case study. At the opposite end of the spectrum, patients with mild hemophilia and factor levels between 6% and 40% typically only bleed with more severe trauma.

That being said, clinical experience shows that individuals with various factor levels and various phenotypes of hemophilia bleed differently. So I think the trend over the past few years is to individualize therapy for the patient and treat to whatever level is necessary to prevent bleeding episodes. Obviously this is going to require a patient who’s very involved and dedicated to their care, because the only way we can tailor therapy is if they come and get factor levels drawn at different points to determine their factor half-life and pharmacokinetics. There are a lot of aspects involved in logistically accomplishing these studies and subsequently having patients remain adherent to their treatment regimen. Prevention of bleeds is the overall goal. Therefore, whatever factor level is required to prevent bleeds is what we aim for in terms of the trough factor level.
How do you weigh the benefits of an active lifestyle against the disadvantage of a potentially greater number of bleeds?

JONATHAN ROBERTS, MD: You look at quality of life studies and joint health studies, and what those studies show is that people are happier when they’re more active. Furthermore, their long-term joint health is better when they have lower BMIs and improved cardiovascular health when they’re active. We really only prevent our patients from participating in very high-risk activities, such as American football, lacrosse, ice hockey, and other contact sports like that. Basketball is definitely a contact sport, but it’s a moderate contact sport, so if that’s what he enjoys doing and he’s going to have a happy, more productive life doing it, then we adjust treatment to his lifestyle. I think that there’s more harm to be done in not allowing patients with hemophilia to do the things they enjoy. The result may be depression or obesity, which is already a problem in America and is even more difficult to manage as patients with hemophilia get older because of limited mobility. So if we can prevent the patient from having bleeds and they’re adherent to the treatment regimen, I think it’s worth the extra cost of treating them more aggressively because they’re going to have a better life.

Patients who are insistent on participating in high-risk activities can present a real clinical challenge. We just talk with them openly and tell them how we perceive the bleeding risks of whatever activity they’re considering. I know what touch football ended up being for me when I was a kid, and I don’t think that’s really changed. I talk with them about the potential of bleeding with high-risk and moderate-risk activities. You have to walk the fine line of not necessarily endorsing a specific activity, but encouraging adherence to prophylactic or on-demand factor therapy. These can be really difficult conversations.

Patients come to us and say, “You told me not to play street hockey, but I did it anyway and I got a bleed.” They’re still our patient and we’re still going to take care of them. We have to advocate what we think is best. At the same time, we also have to really help them take their healthcare in their own hands and say, “Look we’re here to support you, to be advocates for you in how to live the best life you can with your bleeding disorder.” Some of this is going to be on the patient. We can’t be with them 24/7. So really, it’s a case-by-case discussion. Especially in adolescents when patients are trying to learn what it’s like to be an individual. Sometimes mom and dad may be overprotective or they may not be protective enough. It’s definitely a case-by-case discussion and it can be really difficult.
I think the easy questions are the things that all hemophilia providers agree on, like full contact football and ice hockey. It’s these gray areas where we really have to talk to patients and counsel them on an individual basis. We let them know that, at the end of the day, if they’re going to be doing something that’s a little higher risk, they should be infusing right before that activity even if we’re not going to give them the green light for it.

**Do payers regularly monitor or even place restrictions on dosing that they would consider to be excessive? How are these determinations made and what kind of information do you require from providers in these situations?**

**CELYNDA G. TADLOCK, PHARMD, MBA:** It really goes back to the individual patient case. Of course, there’s going to be a discussion about the rationale behind the treatment approach. Why does this patient require more? And it’s going to come down to that patient running and enjoying an active lifestyle. What’s going to be needed for that particular patient situation? For us, this discussion occurs between experts within our National Medical Excellence Program in hemophilia and the prescribing physician and the HTC.

**Describe the kinds of specialty management interventions/approaches that may come into play if this patient were to receive his factor through a specialty pharmacy.**

**MICHAEL ZEGLINSKI, RPH:** Specialty pharmacies have been able to assist in these scenarios by working with the treatment center and the payer. In many cases the pharmacy is speaking with the patient quite often. It could be weekly, every other week, or monthly. And it may be that the health care professional who’s having the most frequent conversations with the patient best understands what’s going on. There might be nurses going to the patient’s house to administer the infusions that understand the home life, that have seen the home, that have seen the family situation, and can provide additional insight to the payer to explain why these differences exist and why there’s a need for more factor in certain situations. In this manner, representatives from the specialty pharmacy can really tell the story of this patient as an individual and why there’s a difference here.

That’s what I’ve seen as being one of the very positive collaborative aspects of the interactions of pharmacies.
with payers and prescribers: that there’s a real-life view of the patient from actually being in the patient’s home or at their place of employment. It’s a unique perspective that allows the specialty pharmacy staff to truly understand the patient. Telling that story that’s not in a clinical chart is very helpful to explain differences in treatment approaches and the rationale behind them.

Case #2: A 4-year-old Male with Severe Hemophilia A and an Inhibitor

- Developed an inhibitor at age 2
- rFVIIa was also used to provide perioperative hemostasis for placement of a subcutaneous port to facilitate regular factor FVIII infusions for ITI, which eradicated the inhibitor
- 3x weekly rFVIII prophylaxis initiated at age 3 after his parents had been trained by the HTC nurse to infuse at home due to his level of activity

What factors play a role in determining successful ITI therapy? Can you please explain the role of bypassing agents in the management of inhibitors and how the decision is made between ITI and the use of bypassing agents?

JONATHAN ROBERTS, MD: As I mentioned previously, the main factor contributing to successful ITI therapy is patient compliance with the treatment regimen, which can be exceedingly difficult to follow. In ITI, daily factor infusions are given to expose the immune system to the factor consistently and essentially “teach” the immune system over time to become tolerant to the factor and not elicit an immune response. The result is immune system tolerization and the factor can be successfully used for prophylaxis in future bleeding episodes.

Bypassing agents with inhibitors are very important and there’s actually a lot of data that has recently shown that prophylaxis with bypassing agents—whether it be activated prothrombin complex concentrate (aPCC) or recombinant FVIIa—is efficacious for preventing bleeds and maintaining joint health in patients with inhibitors. This is obviously an already expensive condition, but when you add daily factor VIII replacement for
ITI and also treating either daily or every few days with bypassing agents to prevent bleeds it can get astronomically expensive. But again, there are data to support that this approach is best for patients’ overall long-term joint health.

The decision between ITI and the use of bypassing agents is fairly simple. For us, if a patient is on ITI and they’re having breakthrough bleeds, then we discuss prophylaxis with a bypassing agent. If we’ve done ITI for a few years and there’s really been no change in their inhibitor and we’ve tried other agents, such as rituximab or other immunosuppressive therapies, then bypassing agents become a routine consideration. We have adult patients that essentially gave up on ITI after a period of years and are treated exclusively with bypassing agents. That’s not the best-case scenario, because we know that the best replacement therapy is the protein that the patient is missing. You can achieve hemostasis with bypassing agents, but it’s not always optimal. It can be a very challenging clinical treatment scenario.

Does a case such as this, which includes a costly ITI regimen followed by routine prophylaxis, raise any sort of red flags during the claims adjudication process? What kind of communications take place between the payer representatives and HTC providers for members who require this intensive level of services?

CELYNDA G. TADLOCK, PHARMD, MBA: When the prescriptions come in for coverage they proceed through the precertification process as usual. But yes, because of these unique situations certainly we’re going to have an active dialogue between the utilization team at the treatment center and our National Medical Excellence Program to evaluate this patient’s case individually. We do have some criteria that apply relative to ITI induction and intensive dosing during that phase. Those cases do go through re-review every six months if the patient needs to continue. ITI warrants a more in-depth review rather than issuing a one-time precertification.
Clinical Updates in Hemophilia Managed Care and Specialty Pharmacy to Improve Cost-effective and Comprehensive Care

Case #3: A 48-year-old Male with Mild Hemophilia B

- Lives in a rural area that is an hour away from the nearest hospital and two hours from his HTC
- Rarely requires on-demand factor, but is charged a $500 copay to receive factor in the ED
- Prescribed to have 2 doses of factor in his home at all times, arranged and dispensed through a specialty pharmacy
- Later required knee surgery for arthropathy and the specialty pharmacy likewise delivered a continuous infusion pump and trained him in its use for postsurgical prophylaxis at home for a week after surgery

In terms of shelf-life, discuss the stability of factor doses for infrequent, on-demand infusers. Mention anything that can be done to manage these patients by ensuring the patients don’t stockpile doses, etc. Describe any documentation payers require for additional factor to be dispensed/shipped.

MICHAEL ZEGLINSKI, RPH: In terms of the shelf-life of the product, the stability of those factor doses for infrequent, on-demand infusers is definitely a concern. It’s something that I’ve seen and with which we’ve been challenged. From the standpoint of managing patients with these doses, making sure they don’t accumulate an oversupply and making sure they’re used before they expire can be challenging. Anytime we encounter people in the mild-to-moderate range that do not infuse often, ensuring that they have product on hand is one of our primary aims, especially if they live in a rural areas or don’t have easy access to medical treatment. This in itself can be a challenge, considering some of these patients are not self-infusers because they don’t infuse frequently and perhaps never even learned to infuse. Many of these patients also don’t have a nurse nearby or someone in the family that can administer the infusion.
In prior years this was a very big problem when there were factor shortages and assay sizes were not as plentiful as they are today. The product would be provided and then would unfortunately expire. I suppose it’s fortunate from a standpoint that the patient didn’t have any bleeds and didn’t need it. However, it’s unfortunate that someone paid for the product and it didn’t get used. Again, these scenarios were more of a reality in the past.

What we’re seeing today is that we have more options; specifically, we have products with longer shelf-lives. And while this is still a challenge because we do have people that are infrequent infusers and the product may expire, we see it happening much less frequently today than what we’ve seen in prior years. Specifically considering the need for the patient in this case study to use a pump is something that’s a bit unusual. They rarely infuse and now, because of a surgery, need to have a continuous infusion pump.

In these cases, what we’ve found is that providing nursing support is critical. Specialty pharmacies have done a very good job of ensuring that while somebody is on treatment for a week, such as this particular patient, there’s very intimate support from nursing and from daily phone calls or discussions with the pharmacy to guarantee that the therapy is going as expected. We’ve also seen that the payers want to know that there are appropriate safeguards in place to ensure that, if they’re going to pay for the therapy and the pump, the patient is going to receive it successfully. So we provide a lot of that ongoing support in the cases of patients such as this one.

Just getting to the patient can be a challenge at times. When you have people in rural areas, driving there is one thing. But during the winter I’ve seen extremely challenging cases of patients who live in remote areas that are mountainous and there’s a lot of snow. It’s just getting the appropriate staff to the patient, or getting the patient out of their home to medical treatment, that has been challenging. Still, we find a way to assist these patients because this therapy is not optional.
Do plans have specific criteria in place in terms of the number of factor doses allowed to be kept in the home? If so, how do you determine that number? Do you require documentation of a bleed to ship additional factor?

CELYNDA G. TADLOCK, PHARMD, MBA: Because it is so highly individualized, we don’t have specific criteria that limit the number of factor doses that can be kept at home. Instead, what we’re actively doing is monitoring for any spikes that we do see in terms of utilization. Such a spike may result in some type of intervention like an outreach to the patient, the supplier, or the treatment center.

However, limitations are really established with patients based on their individual needs. So there’s no one standard number of doses that can be kept at home that applies across all patients. Instead, it’s calculated in collaboration with the treatment center based on what is rational for that patient’s needs. Then, if there were to be a spike in utilization, that ideal number is going to guide us toward an intervention or an outreach.

MICHAEL ZEGLINSKI, RPH: Again, I think it goes back to what we discussed earlier: communication here is really key. If factor is prescribed, the product is ready to be dispensed by the pharmacy. Communication and the rationale for a specific therapeutic course being provided to the payer is very critical element of the whole process.
Can you please briefly describe the predominant perisurgical considerations for patients with hemophilia?

What factors determine dosing and administration specifics in pre- and post-operative settings? What is the ideal number of doses to have on hand in this situation and what determines this number?

JONATHAN ROBERTS, MD: As was mentioned earlier, the shelf-life of factor concentrates is now usually multiple years if the doses are kept refrigerated. And for this patient, the use of a continuous infusion pump in this situation would be very unique. I agree with the specialty pharmacy opinion that home nursing support would be critical in this patient’s case. I know our HTC would have someone out there at the house, because most times using continuous infusion we would keep these patients in the hospital and come up with some sort of bolus regimen for prophylaxis.

In terms of perisurgical considerations, I think it’s important for people to realize that you don’t just need factor therapy at the time of surgery. Factor replacement is very important for wound healing. And so a lot of times, when we have patients who have had major surgeries, we like to keep factor trough levels above 50%. You basically want to keep the patient at near-normal levels. That’s important for a variable period of time depending on the surgical procedure that the patient underwent.

Dosing and administration is determined by factor recovery in routine half-life studies for patients while they’re in the perioperative setting. We check their baseline factor levels prior to surgery and we check the level after we’ve given them their preoperative dose to determine their peak level. Next, we actually do a real-time pharmacokinetic (PK) study in the patient, measuring trough levels prior to doses and tailoring the patient’s therapy to our desired trough level. So if someone has a severe central nervous system bleed or surgery, like a spinal surgery, we’re going to want to keep trough levels even higher, at 75% or 100%. That’s where continuous infusion in the hospital setting really comes into play.

We’ve touched upon this multiple times, but it’s really tailored to the individual patient. Disease severity, past history and bleeding phenotype, and the specific procedure being performed all come into play. For these reasons, I think it’s vital to have an HTC involved in the decision-making process.
In terms of the ideal number of doses to have on hand, it again comes down to decision tailored to the specific needs of the patient. I think for most people with mild disease, like the individual in this case study, having two emergency doses on hand is adequate in the majority of scenarios. But again, if the patient bleeds more frequently, you need to adjust the number of doses that are kept in the home. Our severe patients on prophylaxis are typically getting approximately 15 doses to be kept at home on a routine basis. Of course that can vary all depending on the number of bleeds. These considerations represent the active discussions that have to happen between the care providers, the pharmacy, and the insurance companies.
Do you have any final words for payers and providers in summation of this roundtable discussion?

JONATHAN ROBERTS, MD: It’s an exciting time to be a hemophilia provider and to be working towards improved therapies for individuals with bleeding disorders. And I think that having open discussions like we’ve had here represent a crucial element for ensuring that we can provide patients with optimal care that’s cost-effective and that allows patients to lead a fulfilling life without bleeds.