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Practical Guidance for Surveillance and Reporting in Hemophilia A

Announcer:
Welcome to CME on ReachMD. This activity, entitled "*Practical Guidance for Surveillance and Reporting in Hemophilia A,*" is provided by Prova Education and is supported by an independent educational grant from Genentech.

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Here's Dr. Shannon Meeks

Dr. Meeks:
Pharmacovigilance is essential for identifying new, rare, or serious adverse drug reactions or ADRs. Pharmacovigilance is also needed to ensure the safe and efficient use of therapeutic agents and appropriate patient populations. So how can you apply these pharmacovigilance principles and processes to everyday clinical practice?

This is CME on ReachMD, and I'm your host, Dr. Shannon Meeks.

Dr. Roberts:
I'm Dr. Jonathan Roberts.

Dr. Meeks:
Okay. To start things off, Dr. Roberts, can you please give us an overview of treatments used for the management of hemophilia A? And really, is there any available real-world evidence to tell us about the safety and efficacy of these treatments?

Dr. Roberts:
Yeah. Absolutely. So, you know, there are, thankfully, many different options now for patients for treatments in hemophilia A. You know, I think traditionally, we've used standard half-life factor products, and then moving more recently to extended half-life factor products. And now we're actually in the era where we have non-factor products, such as emicizumab and others that are in development, that are really transforming the management of hemophilia A.

So all of the products currently on the market are safe. For the factor-based therapies, we worry about inhibitor development, which we are consistently evaluating our patients for. And then also different types of allergic reactions that can happen, whether it's either to the components in the factor products, such as some of the stabilizer products like PEG or other things. And certainly, allergic-type reactions can also happen with some of the newer products like emicizumab.

Dr. Meeks:
No, I agree. I think that, you know, we've got a long track record of looking for adverse reactions and what's happening with our factor products, both the traditional recombinant and plasma-derived factors, as well as the extended half-life factors. And I think one of the reasons that we really wanted to do this CME today was to give ourselves an opportunity to think about – as we start seeing emicizumab, the first non-factor product approved and potentially the first of many non-factor products in gene therapy, and other novel treatments in which we will, again, need to focus in on adverse drug reactions and reporting and what that means both to our patients but also to the community as a whole.

So the next question I have for you is with this overview in mind, what are some of the more common adverse events that are seen with these agents?

Dr. Roberts:
Sure, very good question. So, you know, for the standard half-life and extended half-life factor products, we are always vigilant to evaluate for inhibitor formation. So whether the factor's not working as well or if a patient is experiencing breakthrough bleeds despite their treatment, those usually signal that we need to look for inhibitors. And we do that at baseline anyway, at least once a year. Sometimes, also, different reactions can occur to different components of the factor products that aren't the factor specifically, such as the PEGylation or other components. And so that always needs to be evaluated and, certainly, if any reactions occur, directed to the treatment center.

In the non-factor therapies, especially in the HAVEN trials with emicizumab, we did see that there were some thrombotic events and thrombotic microangiopathy that occurred when patients also were being treated with activated prothrombin complex concentrates. So this was really in the setting of patients with inhibitors that were being treated with emicizumab as prophylaxis. And since then, we've also seen some other thrombotic events, so thankfully, these have been infrequent. And certainly, the pharmacovigilance process is imperative to report these events so they can be studied and understand how to mitigate risk in all of our patients.

Dr. Meeks:
Thanks, Dr. Roberts. And I agree, you know, I think we, as a community in hemophilia and as practitioners, we're really good about reporting our adverse events on the clinical trials. And I think some of the points that we really wanted to come out of this CME that you heard about earlier with Dr. Leissinger is what adverse events, you know, when they happen outside of clinical trials – obviously the adverse events that happened within clinical trials can happen outside of the trials, but as more and more people are exposed to a drug with many other drug combinations, new adverse events can happen as well.

Dr. Roberts:
Absolutely. I think it's very important that we continue to have good pharmacovigilance. I know we do so in our clinics, and our colleagues across the country and really across the world do, as well. So if some sort of adverse event happens that may be associated with medication, it's always important to report it to the manufacturer and have an appropriate process at your individual institution so that we can evaluate those instances and understand them and hopefully prevent them from happening in the future.

Dr. Meeks:
For those just tuning in, you're listening to CME on ReachMD. I'm Dr. Shannon Meeks, and here with me today is Dr. Jonathan Roberts. We're discussing the important role of pharmacovigilance in the management of hemophilia A.

Now that we have a better understanding of adverse events that can happen with some of the novel therapeutics, Dr. Roberts, can you shed some light on strategies for surveillance and monitoring of both treatment response and adverse drug reactions?

Dr. Roberts:
So, that's a really great question on surveillance. I think it's really important that patients and families develop a system that works for them monitoring their prophylaxis and recording any type of bleeds or additional treatments that they may need. Traditionally, there's been paper records that patients have done, or there are mobile apps that are now available that really allow the patient to directly communicate with their treatment center and provider, as well as show additional details like images of their bleed and any other adverse reactions that may happen. And certainly, strengthening that communication between patient and the treatment center or provider is imperative so that we can have good, continued surveillance of the efficacy of their therapy and also monitoring the safety of their treatment and capturing any adverse reactions that would occur.

Certainly, if any adverse drug reactions were to occur, the pharmacovigilance process would be implemented and the manufacturer notified so that these types of instances can be reduced and treatment strategies can be developed.

Dr. Meeks:
I agree. I think one of the things that's helpful on some of the mobile apps is that if a patient reports a new adverse event that we haven't seen much of, oftentimes the providers are getting notified in real time rather than waiting for them to come to clinic and get that done.

Now, let's apply this information using a case. Here's the case for today: a 13-year-old patient with hemophilia notifies you that he's having a localized reaction after receiving his emicizumab injection. In fact, he actually got his injection yesterday, and his localized reaction is starting to calm down. He was talking with his specialty pharmacist today to reorder his next dose and mentioned that this reaction had occurred, and they encouraged him to report it to the treatment center, as well. So he now has reached out to the treatment center, and Dr. Roberts, a real question for you is what, at the treatment center, would you do to start this pharmacovigilance process, and how is that process implemented in your everyday patient care?

Dr. Roberts:
Yeah, very good question. So this type of information would, first of all, go immediately to one of the providers, so one of our physicians here and nurse practitioners. And interestingly, in the emicizumab trials, local site reaction did occur about 20% of the time. And the good news is over 90% of the time, it resolved without treatment. A majority of those patients simply had some redness at the injection site, but some did also get pruritic or itchiness at the site. And so typically, our protocol would be to recommend a pre-dosing with diphenhydramine or Benadryl to help with the itchiness and really watch and monitor the site. Thankfully, we've not seen repeat or refractory cases of local reactions like this happening. But in that, still, having good pharmacovigilance means that we would track that that reaction happened and implement the process to notify the manufacturer so that we can follow up and make sure that we're not seeing a change in what was reported in the clinical trials and certainly that no other associated reactions happened, as well.

Dr. Meeks:
Right, and I think for cases like this in terms of the pharmacovigilance, it's also important to have some observation potentially at the next dose, and if hives were to develop, to further update that pharmacovigilance process to say this is what happened next.

Well, this has certainly been a fascinating conversation. But before we wrap up, Dr. Roberts, can you share your one take-home message for our audience?

Dr. Roberts:
So I think it's really important that patients with hemophilia A tailor their management to their individual goals and to really be in close contact with their provider to discuss what type of therapies work best for them, especially as we're entering this era with many different options of both factor-based and non-factor-based therapies and even gene therapy in the near future. It's also important to recognize that patients' needs may change in different seasons of their life, so this should be an ongoing and active discussion with their provider.

Dr. Meeks:
I completely agree, Dr. Roberts. I think the one message I would add is just to really encourage the patients and families as they grow through the lifespan to have a system that they develop to record what's happening, whether it's calendars, paper, mobile apps, to really be sure that they're able to track and report what's happening.

Unfortunately, that's all the time we have for today, so I want to thank our audience for listening in and to thank you, Dr. Roberts, for joining me and sharing all of these valuable insights. It was great speaking with you today.

Dr. Roberts:
Absolutely, my pleasure. Thanks.

Announcer:
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