

PROCEEDINGS:

ASSESSING PHARMACISTS' AWARENESS OF THE FOLLOW-ON INSULIN MARKET, NONMEDICAL PRODUCT SWITCHING, AND ITS IMPACT ON PATIENT CARE





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INTRODUCTION

Diabetes is a prevalent and costly disease that is challenging to manage. There were approximately 30 million individuals in the United States with diabetes in 2015, and the annual costs of diabetes were estimated to be \$245 billion in 2012.^{1,2} Diabetes is a complex and multifactorial disease that requires patients to take an active self-management role to prevent both acute and long-term complications.

A large body of research has demonstrated that pharmacists' delivery of patient care services can improve outcomes for patients with diabetes. In current pharmacy practice, pharmacists in diverse settings provide a wide range of services to support patients with diabetes in managing their conditions and addressing their health care needs. The continuum of services includes activities such as:

- Medication counseling
- Immunization services
- Education on diabetes self-care skills
- Targeted pharmacy-based services such as blood glucose meter training, insulin pump training, foot care, wound care, etc.
- Comprehensive diabetes self-management education
- Protocol-driven medication management under collaborative practice agreements (CPAs) such as ordering lab tests, monitoring medication, changing medications, etc.
- Independent direct patient care

Pharmacists are key members of the patient-centered health care team for individuals with diabetes and other chronic conditions. A December 2016 consensus consortium of experts in diabetes care convened by the American Pharmacists Association (APhA) Foundation on *Value-Based Health Benefit Design Considerations in Patient-Centered Team-Based Care* has recommended six key principle-centered themes for transforming the delivery of patient care:

- **Inspire** patients, providers, and payers to transform the health care system
- **Make** the patient the center of all health care decisions
- **Promote** access to evidence and information that elevates clinical decision making
- **Align** the incentives for patients, providers, and payers
- **Cultivate** quality improvement and practice enhancement
- **Take** accountability for the financial, clinical, and humanistic outcomes of patient medication use

The consortium noted, "The goal of delivering high quality health care services that result in positive patient outcomes while minimizing health care costs is difficult to achieve or evaluate because the health care system is complex and involves numerous stakeholders that each have their own vested interests in the system." While recognizing patients are interested in affordable, quality services that enable them to manage their health, the consortium notes there are obstacles within the

health care system that can interfere with patient self-management, including high costs of care, formulary restrictions (such as prior authorizations), or lack of benefits/coverage for recommended treatments. Participants noted disruptions in care (such as nonadherence, formulary changes, or annual changes in health benefits/coverage) can substantially interfere with the patient's ability to maintain control of chronic health conditions. They recommend that to optimize care for patients, unnecessary barriers and disruptions in care need to be eliminated or minimized so patients can be consistent with their treatment plans and achieve the best possible outcomes.

The consortium discussed payer decisions that may affect a patient's benefit and coverage, recommending they be made based on evidence with the best interest of the patient in mind. A historical framework for formularies was provided and the participants noted, "In the current system, stakeholders involved in making formulary decisions may not be actively involved in the patient care process and may be engaged in a 'national' approach to formulary management, moving away from local/regional decision making. This can cause a potential negative impact on patient care."

This approach to benefit management has occurred with numerous drug classes to treat chronic conditions and seems to be occurring more frequently. Most recently, the diabetes treatment market has been impacted by nonmedical switching of therapies. Nonmedical switching is defined as when an insurance plan excludes a drug from its formulary and forces the patient to be switched to an alternate therapy.

Expanding Treatment Choices for Diabetes

New emerging insulin therapies and the introduction of follow-on biologics have led to more treatment choices for patients with diabetes. In addition, because insulin and insulin analogs

are biologic products, they may be joined on the market by biosimilar and follow-on biologic insulins when they lose patent exclusivity.

Biosimilars and follow-on biologics are biologic products that are highly similar to already approved biologic products. Biosimilar products are not "generic" versions of biologic products; they undergo a different regulatory pathway that accounts for important distinctions between biologics and small molecule drugs. Biosimilar products must demonstrate that they are highly similar to the reference product with no clinically meaningful differences in safety and efficacy. Biosimilars are expected to be less expensive than the reference product and may offer the potential to reduce costs and improve patient access to biological products by increasing treatment options and creating a more competitive market. The U.S. Food and Drug Administration determines whether a biosimilar is interchangeable with the originator product and if the biosimilar is interchangeable, it is listed in the Purple Book.

The first biosimilar in the United States was approved in 2015, followed by three more in 2016 and two more in 2017. Because insulin and insulin analogs are biologic products, they may be joined on the market by biosimilar and follow-on biologic insulins when they lose patent exclusivity.

In 2015, Lantus (insulin glargine) was the first insulin analog to lose patent exclusivity, and Basaglar, a new version of insulin glargine, was approved in the United States in December 2015. Basaglar has been approved as a follow-on biologic. Basaglar is often mistakenly referred to as a biosimilar. It is not. A follow-on biologic is similar conceptually to a biosimilar, but uses a different regulatory pathway.

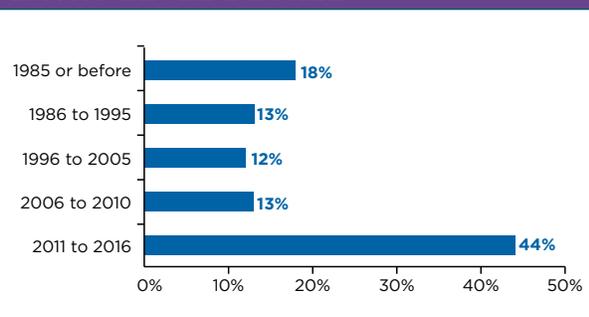
Many other biosimilar insulins are in development and are likely to enter the market as more patents expire in coming years. The increasing number of insulin products on the market may pose challenges for patients and health care providers, particularly if there are questions regarding how to switch

among products. As an example, from a regulatory standpoint, Basaglar is not an AB-rated product that can be substituted for another insulin glargine such as Lantus. However, many health plan and pharmacy benefit management (PBM) formularies have made the decision to substitute follow-on insulins.

Because of these trends, APhA conducted a survey in 2017 and convened a virtual advisory panel to characterize pharmacists' understanding of follow-on insulins, the nonmedical switching that occurs with these products, their concerns about the practice, and its impact on patient care and outcomes. A total of 364 pharmacists responded to the online portion of the survey and an additional 8 pharmacists participated in the APhA Follow-On Insulins Virtual Advisory Panel. Survey respondents were in practice an average of 13 years (Figure 1) and were from all areas of the United States (33% South, 29% Midwest, 19% Northeast, 17% West, 1% Puerto Rico, and 1% outside the United States) and practiced in a variety of pharmacy settings (21% chain pharmacy, 16% independent pharmacy, 11% hospital/institutional inpatient pharmacy, 10% academia, 9% ambulatory care clinic pharmacy, 8% supermarket pharmacy, 4% physician office-based practice, 4% outpatient clinic pharmacy, 3% mass merchant pharmacy, and 14% other).

Participants in the advisory panel included frontline pharmacists practicing diabetes care in mass merchant (1), supermarket/grocery (2), independent (1), ambulatory care (3) and specialty pharmacy (1)

FIGURE 1. YEAR SURVEY RESPONDENTS RECEIVED ENTRY-LEVEL DEGREE



with representation from 7 states in the Midwest (1), South/Southeast (3), and Western/Southwestern (4) United States to collect the desired data. The participants varied in years of practice experience from 5 to more than 30 years, with most in the 15- to 20-year range across a variety of practice settings.

Diabetes Management in Participants' Practices

Pharmacists responding to the online survey and those on the advisory panel reported providing a variety of services for patients with diabetes, reflecting the continuum of services noted earlier:

- Medication counseling
- Immunization services
- Education on diabetes self-care skills
- Targeted pharmacy-based services such as blood glucose meter training, insulin pump training, foot care, wound care, etc.
- Comprehensive diabetes self-management education
- Protocol-driven medication management under CPAs such as ordering lab tests, monitoring medication, changing medications, etc.
- Independent direct patient care

Four members of the advisory panel practice under a CPA that allows them to change therapies for patients with diabetes (and other chronic conditions) while 22% (n=79) of survey respondents reported doing so. Fifty percent of respondents report more than two-thirds of their patients are treated under these agreements with fully 35% of respondents reporting that 96% to 100% of their patients are treated under these agreements.

Incidence of Nonmedical Switching and Follow Up With Prescribers and Patients

Advisory panelists and survey respondents reported a significant increase in nonmedical switching of diabetes therapies (Table 1), especially insulins and glucagon-like peptide 1 (GLP-1) agonists (Figure 2). Advisory panelists expressed frustration over the increase, noting that “we are definitely seeing more in the last few months than the last 2 years.” One advisory panelist noted that two major insurers in her market changed formularies from Lantus to Basaglar. Another advisory panelist noted that nonmedical switching is not new and provided examples when more statins or dipeptidyl peptidase (DPP-4) inhibitors were introduced to the market. Another noted, “The analogy that I use in this time of all these new insulins being available is we have three rapid-acting insulins—Humalog, NovoLog, and Apidra. This nonmedical switching was happening with those products prior to the newer insulins. A plan might have Apidra but not Humalog, or they switched in January and now the patient needs to be switched to the rapid acting. From a kinetics standpoint, they are all pretty similar, maybe perhaps not quite in a pump patient. So this nonmedical switching in my opinion is not new. It is more frequent now because of the high-concentration insulins that have come out, and now with Basaglar.”

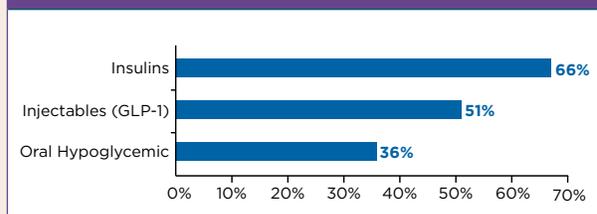
This formulary change often results in the pharmacist informing both the patient and the prescriber of the need for a change (77% of survey respondents). Pharmacists practicing under CPAs will make the necessary change to the patient’s therapy based on formulary coverage. Those not practicing under CPAs most immediately need to inform the patient and then the prescriber to get a medication switch initiated. This requires a note in the electronic patient record, a phone call, or a fax to provide treatment options. If the

TABLE 1. INCIDENCE OF NONMEDICAL SWITCHING OF DIABETES PHARMACOTHERAPY

Are you seeing an increase in the incidence of non-medical switching for diabetes pharmacotherapy over each of the following time periods?

	n=	Yes	No
2014 vs. previous years	184	28%	72%
2015 vs. 2014	139	52%	48%
2016 vs. 2015	268	79%	21%

FIGURE 2. DIABETES PHARMACOTHERAPIES MOST IMPACTED BY NONMEDICAL SWITCHING (N=296)



prescriber chooses to keep the patient on the original therapy, then a prior authorization process is initiated. As one respondent noted, “We explain that the patient’s insurance does not cover the medication that they prescribed and there is another medication in the same drug class that is covered. We ask them to evaluate if this alternate drug is an acceptable alternative for their patient. If it is not, we ask them to contact the insurance company for prior authorization to cover the original medication.”

Another advisory panelist, who works in a specialty pharmacy practice, noted having agreements with pharma companies that compensate them for the prior authorization process. Another noted an innovative Medication Access Resource Center within the practice’s integrated health system that has sped the prior authorization process.

Prescriber Reaction to Nonmedical Switching

Prescriber reaction to nonmedical switching varies. Survey respondents were asked: “When you need to consult with prescribers regarding a nonmedical switch, how do the doctors usually react to the required switch?” Results from this question are shown on Figure 3.

One advisory panelist reflected, “The endocrinologists I practice with are pretty much up to speed on the different products. With our primary care providers, this practice has added tremendous confusion. When the new GLP-1 receptor agonists–basal insulin combinations are approved and marketed, it will be even more confusing to them.”

Proactively, advisory panelists report doing much more physician education about new diabetes therapies, their advantages, appropriate use, patient transitions, and coverage issues. Both advisory panelists and survey respondents noted the need for a variety of educational aids and resources to assist with this outreach. Advisory panelists say the more education they provide, the more often primary care providers express the desire for a pharmacist to be in the clinic on the health care team—a positive outcome for pharmacy.

Patients are informed of the need to change therapy in a number of ways (Figure 4).

Advisory panelists noted therapy changes can create delays in patients receiving their medications depending on the lead time with which the patient requested a refill. Often medication therapy changes may take up to 3 days. Seventy-eight percent of the survey respondents report their patients with diabetes experience a delay in acquiring the alternate therapy when a nonmedical product switch occurs. Respondents who reported their patients experience a delay, indicated the delay ranged from less than 24 hours to more than

FIGURE 3: PRESCRIBER REACTION TO NONMEDICAL SWITCHING” (N=287)

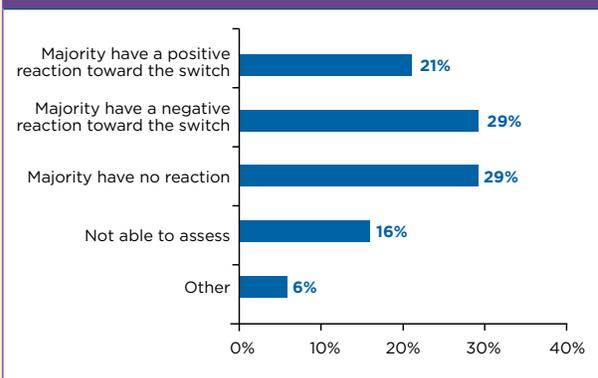


FIGURE 4. HOW PATIENTS ARE INFORMED OF NONMEDICAL SWITCHING OF THEIR DIABETES PHARMACOTHERAPY (N=296)

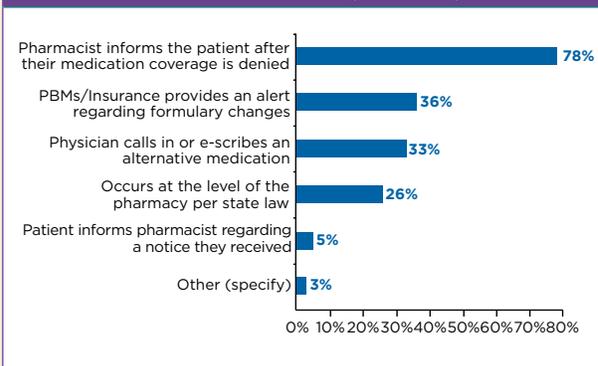
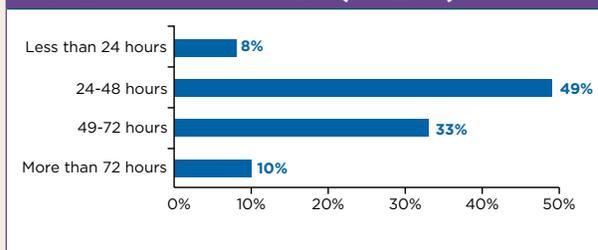


FIGURE 5. LENGTH OF DELAY IN THERAPY DUE TO NONMEDICAL PRODUCT SWITCHES (N=203)



72 hours. (Figure 5).

Patient Reaction to Nonmedical Switching

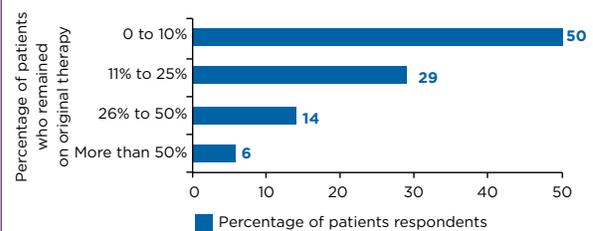
Patients' reactions to the nonmedical switching may vary. The majority (81%) accept the switch, while 9% choose to stay on their therapy. Online survey respondents note that patients "accept the switch but are very frustrated over the switches and changes to their routines, are often unhappy and reluctant."

One advisory panelist noted from the patients' perspective, they may be adherent to their current therapy and now a wrench is thrown into their self-management system that can impact their diabetes control. Concern about experiencing hypoglycemia is often the result. Patients are also concerned about the gaps in their care and require reassurance from the pharmacist about the new therapy. Another said, "You do see a lot of frustration and misunderstanding when they have been on something and then they are being forced to switch. The whys and the how this will affect them, and what they need to do in the interim is always very concerning to the patient." Another said, "People have a very personal relationship with their insulin. They are very nervous about switching to something else because they don't know what it's going to be and it is getting used to something new." Another noted having patients who are so attached to their vial and syringe therapy that they don't want to move onto an insulin pen, even though most panelists believe this is easier. A survey respondent noted, "Patients complain that they just get controlled on a certain medication without any side effects and then insurance requires them to change agents, which makes them worry. Pharmacists help to assure patients that switching is okay and uneventful most of the time. We also have to answer questions about side effects of the new medication when the patient has concerns."

Sometimes the change can be positive, with one advisory panelist noting improved adherence with a change from twice a day to once a day insulin therapy. One advisory panelist reflected, "Some people are really excited if they get to take basal insulin once a day instead of twice a day." Several noted more flexibility in dosing, administration time for some of the newer insulin therapies, and positive patient reaction.

Change is never easy, but often cost issues cause the patient to accept the nonmedical product switch. Few choose to remain on their current therapy report advisory panelists and survey respondents (Figure 6). Finances play a role in the patient's decision.

FIGURE 6. PERCENTAGE OF PATIENTS THAT REMAINED ON ORIGINAL THERAPY REPORTED BY RESPONDENTS* (N=255)



* Either by paying more out of pocket or physician override/exception/prior authorization.

Panelists said most of their patients cannot afford to stay on their current therapy. Noted one pharmacist, "[Almost] all of my patients have to switch. They don't have a choice." Others noted they will help patients with commercial insurance use patient assistance programs while those with Part D require more assurance.

Pharmacist Concerns With Nonmedical Switching of Diabetes Therapies

Advisory panelists and survey respondents noted a number of concerns and opportunities related to the nonmedical switching of diabetes therapies (Figure 7) and they report that on average it takes them nearly 7 minutes to counsel patients when this type of switch occurs (Figure 8).

Other specific concerns cited by online survey respondents included:

- Adjustment in use of a device they were comfortable with using
- An alternative medication may have special precautions (i.e., increased incidence of bladder cancer) that are not appropriate for the patient
- Change is not person specific, not tailored to the individual; in the future, value-based insurance design may fix this
- Confuses patient
- Different dosing schedules allows for confusion and unintentional adherence issues
- If the patient is well controlled with Medication A, then the patient should be able to stay on A since it works without [adverse drug effects]
- Patient may be controlled on original medication; now with switching, they have to find a new “normal”
- Patient might get frustrated because it destabilizes their sugars for a while
- The time it takes to make this change and the inconvenience to patient, physician, and pharmacist

Moving to alternate therapy may impact glucose control, therapy adherence, testing needs, clinic visits, additional therapy, patient concerns on glycemic control, stress about eating properly and activity level, and even family concerns (Table 2).

FIGURE 7. PHARMACIST CONCERNS ABOUT PATIENTS’ SUCCESS WITH NEW THERAPY

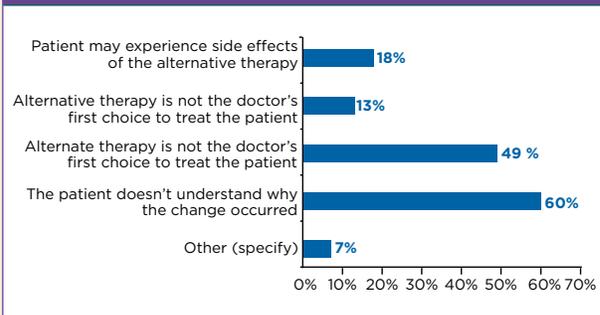
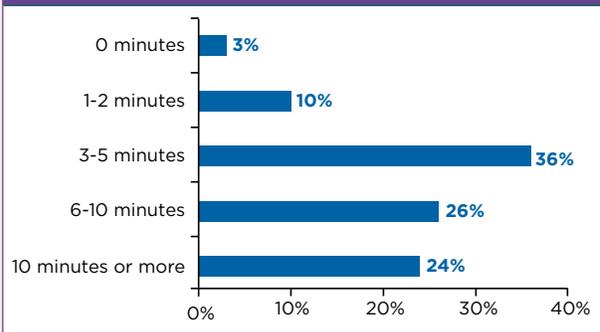


FIGURE 8. AMOUNT OF EXTRA TIME REQUIRED FOR PHARMACISTS TO COUNSEL PATIENTS ABOUT NONMEDICAL SWITCHING OF DIABETES PHARMACOTHERAPY



Advisory panelists were able to offer further insights into the data during their discussion. They noted an increase in resources needed to transition the patient, including more education and clinic visits during the last 2 or 3 years. One noted, “We have had to dedicate more hours from our certified diabetes educator (CDE) staff to address insulin and GLP-1 agonist changes. Our diabetes educators are doing less educating and spending more time fixing medication changes.” The advisory panelist noted significant time re-titrating patients’ diabetes medications to ensure glycemic control when several plans changed coverage from Lantus to Levemir (insulin detemir). They said now they are making similar efforts moving to Basaglar and they are readjusting clinic resources to keep up with this demand. And while medication costs may decline with nonmedical product switches, costs rise for health provider and clinic visits.

TABLE 2. IMPACT OF NONMEDICAL SWITCHING OF DIABETES PHARMACOTHERAPY

How does nonmedical switching impact your patients'...?

	Better	Worse	Increase	Decrease	No Change	Unable to Answer
Glucose Control (n=287)	4%	14%			15%	68%
Adherence (n=287)	5%	23%			29%	42%
Number of Blood Glucose Tests (n=282)			22%	4%	29%	45%
Clinic Visits (n=282)			31%	1%	18%	51%
Hypoglycemia Concerns (n=275)			32%	2%	29%	38%
Diet/Exercise Concerns (n=274)			20%	2%	34%	43%
Anxiety Over New Regimen (n=275)			67%	2%	10%	22%
Family Member Concerns (n=275)			44%	2%	14%	40%
Urgent Care, ER Visits, Hospital Stays (n=273)			8%	3%	19%	70%
Additional Therapy Changes (n=272)			27%	2%	20%	52%

Furthermore, advisory panelists expressed frustration with poor product labeling on dosing titration between agents and an increase in medication errors when patients do not understand that the new therapy replaced a former one (especially during care transitions). “The labeling is conservative and not as helpful with titrating therapies,” noted one pharmacist. Another said, “We can see some more medication errors happening, particularly at the transitions of care, from people not getting their insulin that they were on, from at home, versus dosing changes that might have occurred in the hospital, and those are continued.” Additional patient education is critical. As one advisory panelist noted, “Some people can have a real attachment to their...insulin type, and so it really comes down to patient education, and really spending time on what this new insulin is, how it’s similar, how it’s different, what they can expect. So for me, it’s just been a lot of patient education, and, you know, alleviating concerns.” Use of placebo devices is key to this education, advisory panelists noted, yet their availability can vary widely

across pharmacy settings. An updated resource with the pharmacodynamics and pharmacokinetics of all insulins would be very helpful, panelists said. So would a quick reference card or simple step-by-step instruction card to provide to patients to assist them when they are using the new therapy at home.

On the opportunities nonmedical switching may present, advisory panelists noted cost of therapy may decline with follow-on insulins thereby expanding patient access to treatment; additionally, because of the need to educate patients and re-titration of their dose with alternate therapy, an unintended consequence of nonmedical switching has been re-engagement in self-management and blood glucose testing. On the cost side, several panelists said insulin costs have been rising and with higher co-pays each month, and thus their patients are struggling to maintain their diabetes medication regimens. “It’s having significant impacts on people’s ability to adhere with their therapy,” noted one panel member. Another said, “I absolutely see our role as providing our patients with the most cost-effective medications.” Yet another, “I also

have a hope with the rising insulin prices, especially over the last couple of years, having these newer agents may decrease overall cost for patients who have to pay out of pocket or have no other choice. Ultimately, there may be some light at the end of the tunnel for these drugs.” Lower cost may make access to insulin available to patients who are not currently on therapy and early use can improve disease outcome, noted advisory panelists.

Advisory panelists and survey respondents also believe the additional time and resources that are being put toward implementing nonmedical product switches should be reimbursed. Fully 96% of online survey respondents agreed that reimbursement should occur. “This issue presents more roles and opportunities for the pharmacist and we should be getting paid for these services,” noted one panelist.

Conclusion

Advisory panelists concluded that the increasing use of follow-on insulins and nonmedical product switching present “an opportunity to re-educate patients, enroll them into diabetes education programs, reinforce testing at home, as well as

talk about switching therapies and the risk of hypoglycemia.” Further, many said it is an exciting time in diabetes therapeutics, yet it can create a lot of confusion among physician prescribers and patients. As one advisory panelist reflected, “The pharmacist can be the person to help reduce that confusion and ensure the appropriate use of all of these new insulins in a very objective, evidence-based, non-biased way; because while the manufacturers do provide great videos, they may send messages of differences among therapies that I don’t always agree with. And the pharmacist can really be that person to translate that information in a very objective way.”

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