
Once-weekly Insulin for Type 2 Diabetes:
Exploring the Science, Clinical Potential, and Practical Considerations
Applications from the [*GSA KAER Toolkit on the Management of Obesity in Older Adults*](#)
Momentum Discussions Podcast from the Gerontological Society of America

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Announcer:

Welcome to the Gerontological Society of America's Momentum Discussions, where we explore groundbreaking topics in the field of aging.

Jen Pettis:

Welcome to this GSA Momentum Discussions podcast episode titled *Once-weekly Insulin for Type 2 Diabetes: Exploring the Science, Clinical Potential, and Practical Considerations*. GSA appreciates Novo Nordisk's support for today's podcast episode. My name is Jen Pettis, and I'm the Director of Strategic Alliances at GSA. I'm pleased to serve as the host for today's episode. Today's conversation focuses on once-weekly basal insulin therapy for adults with type 2 diabetes. Basal insulin has long been an important option for improving glycemic control. Some people experience practical challenges related to treatment administration, adherence, and long-term persistence with daily basal insulin injections.

In this podcast episode, we'll discuss the science behind once-weekly basal insulin, what clinical trials have shown to date, and how clinicians can think about patient selection, safety, adherence, and shared decision-making when considering once-weekly insulin for people living with Type 2 diabetes.

Jen Pettis:

I'm delighted to be joined by Dr. Rodolfo Galindo, who brings deep expertise in diabetes, insulin therapy, and metabolic health. Welcome, Dr. Galindo, and thanks so much for joining me today.

Rodolfo Galindo:

Thank you very much, Jen, for the invitation. It's a pleasure to be collaborating again with the Gerontological Society of America, GSA, for people who are not familiar with the term. Thank you very much for the work you guys do supporting our older population. It's a great piece of work, and I'm very happy we can discuss the new therapeutics available on the market.

Jen Pettis:

Great. Thanks so much. To set the stage, what are some key challenges adults with Type 2 diabetes may face when starting or continuing daily basal insulin therapy?

Rodolfo Galindo:

Type 2 diabetes is a chronic condition characterized by a progressive decline in insulin secretion. We know that some people will eventually need insulin after a long period of living with diabetes. That need may always be there. There are many options for insulin supplementation, including several basal, long-acting insulins available on the market. The issue is that they impose a significant burden on patients because treatment involves more than the daily injection; it also includes checking glucose, living with diabetes, following dietary recommendations, seeing clinicians, being a person, and having a family. Life is complex. Adding treatment burden is always an issue. We know that many patients do not take their insulin every day, and adherence declines over time.

Especially among older adults, the issue is not simply that someone does not want treatment or that life is too complex. Some people may have limited hand dexterity, which can make it difficult to use a syringe, pen, or dose dial. Others may have limited vision, making it difficult to identify the correct dose. Cognitive impairment, limited access to care, or other circumstances may add further challenges. Although daily injections can improve diabetes management, they can also create treatment burdens and carry risks such as hypoglycemia. In assisted living communities or nursing homes, daily insulin therapy may also increase the care burden associated with finger sticks, glucose monitoring, injections, needles, and pens.

Jen Pettis:

You discussed some of the needs that really led to this once-weekly insulin. What else were researchers seeking to address by developing this once-weekly alternative to daily basal insulin?

Rodolfo Galindo:

Insulin was discovered at the University of Toronto about 100 years ago. That work led to a Nobel Prize and represented one of the breakthroughs in medicine. Since then, a central scientific goal has been to develop insulin therapies that more closely mimic normal human insulin secretion, function, and action. In other words, researchers have sought an exogenous (outside-the-body) insulin that behaves more like endogenous insulin produced within the body. We have excellent treatment choices, but they still do not fully replicate normal physiology.

Insulin concentrations can peak after a dose. When Lantus (insulin glargine) and Levemir first came to market, they were described as having relatively flat profiles. We now know that they still have peaks compared with newer options. That was another reason to develop ultra-long-acting insulins: to mimic normal physiologic insulin function in humans more closely.

Jen Pettis:

How does once-weekly insulin work, and how should clinicians explain its dosing profile to patients in a way that's accurate and easy to understand?

Rodolfo Galindo:

With any new therapeutic, there is a substantial need for education because the treatment is unfamiliar. Clinicians, families, patients, and the broader community all need clear information. Several once-weekly insulins are in development or under regulatory review in different regions. One is insulin icodec, developed by Novo Nordisk under the brand name Awiqli. Its availability varies by country, and clinicians should consult the current prescribing information in their region.

The other one, called efsitora and developed by Eli Lilly, is not yet available; experience with it comes from clinical studies. These are once-weekly injections, and we could say they are very slow-acting; it takes time to reach what we call a steady level, which produces a therapeutic effect. With the first few doses, an additional loading dose may sometimes be needed because the insulin works very slowly. The weekly dose accounts for the total daily dose. One key point in education is that this is not more insulin; it is simply a larger number of units administered once weekly to account for the daily dosing. If a person takes 10 units daily, the weekly dose would be 70 units.

If you do 20, it would be 140. If you do 30, it would be 210. You tell a patient or clinician they need to prescribe 210 units, and they may panic. The right wording is that this is not more insulin or a higher total dose; it is simply a larger number of units because the dose is administered weekly. The weekly dose accounts for the amount that would otherwise be used each day. That is one of the first points to cover when explaining dosing. Over time, some patients may need less insulin when switching from daily insulin, depending on glycemic control. The titration is also performed weekly, or sometimes at longer intervals, rather than daily.

For insulin icodec, the titration used in studies was once weekly. If fasting glucose over the previous 3 days was outside the target range, the dose was adjusted. The studies used specific target ranges, approximately 100 to 130 mg/dL, depending on the study, but that does not mean clinicians will use the same goal in everyday practice. Some patients require higher individualized targets. The bottom line is that when fasting glucose is above target, the dose is increased by 20 units. If fasting glucose is within target, the dose is maintained; if it is below target, the dose is decreased by 20 units, which is approximately equivalent to 3 units per day.

That's what we do with the daily dosing: 20 units up, then 20 units down once weekly. Then you check and try to pay attention to the last three days. Another key point for the once-weekly icodec, Awiqli, is the brand name: if they're using other insulin on days two, three, and four, they may need to slow down on the short-acting because those days work more. The other point is that the first, second, and third doses may not work. You need to create a pool of insulin, especially for people who were insulin-naïve and were not taking insulin. In the first doses, you may see sugar levels run a little high. You could also give an extra loading dose: the first dose would be 210, plus 50% of that (300 units).

The first dose is to build up the insulin dose. If you were using daily insulin and you switched, it's a different situation. A couple of things there. No more insulin, no more dosing, just larger units because it's once-weekly, titration once-weekly, 20 up, 20 down, and then keep an eye on it.

Jen Pettis:

I know there's a lot to talk about and a lot of exciting stuff going on, but what about efficacy? What were some key efficacy findings from the clinical trials when comparing the once weekly versus the daily basal insulin, with adults with Type 2 diabetes?

Rodolfo Galindo:

The trials were designed to compare glycemic control, A1C reduction, hypoglycemia, safety, and efficacy. Both molecules, icodec and efsitora, showed similar A1C reductions. Most studies met the noninferiority goal, meaning that the once-weekly products achieved A1C reductions similar to those of the comparator insulins.

Most of the studies, all of them, had similar situations with hypoglycemia, similar rates of level 2 and level 3 hypoglycemia, which are the hypoglycemia that really matters. We don't have evidence that a week of this would cause more hypoglycemia or lead to higher A1Cs. Just the caveat: the first two, three doses, two, three, four weeks, you may need more loading doses at the beginning, or just be careful, be aware that the sugar may run higher because it doesn't work tomorrow; it works in a week. You need to account for that.

Jen Pettis:

Beyond the A1C reduction, looking at the incidence of hypoglycemia, what other outcomes should be considered and discussed between providers and their patients when they're evaluating their options for basal insulin?

Rodolfo Galindo:

Right, really good. Many of the trials in phase two evaluated what we call PROs, patient-reported outcomes. We wanted to get patient input on whether they prefer this new therapy. That is actually very important because that's what clinicians will do: ask your patients what they prefer. It was pretty good across the board. Many patients, 70, 80, 90% of patients on this, on the studies that were surveyed, say that they would prefer the once weekly, that they would recommend it. It makes sense. In the diabetes clinics, we expect the patients to be the ones driving this. They're going to be coming and saying, "I want that. I want the once weekly. It's just less burden, easier once weekly, one at all." We also have extensive experience with once-weekly GLP-1 therapy, which has been successful in treating metabolic diseases.

Many people are now familiar with once-weekly dosing. Patients are very happy because it's less of a burden. We write prescriptions, but people need to deal with diseases and chronic diseases. The burden of disease is what we always need to keep in mind.

Jen Pettis:

What other clinical factors should the clinician consider when deciding whether once weekly insulin is appropriate for that individual patient?

Rodolfo Galindo:

Yes. For any therapy, new or old, from the last century or the prior century, because the last century was just a few years ago. For any therapy, you need to know that no single medication, therapy, or surgery is the right approach for every patient. Humans are very heterogeneous. We're very different people, even though we sometimes speak the same language. We're different people. You need to know that, and you need to know your patient. You need to be a clinician. You need to know your patient, know what they need, and what they would do. If it's not the best in your mind, it may be the best for what they believe and what they need, the right therapy for the right patient.

Once weekly insulin may not be the right therapy for someone with substantial day-to-day glucose fluctuations or very difficult-to-control diabetes; these patients may need daily insulin adjustments because their glucose is low one day and high the next. A once-weekly dose cannot be adjusted daily. If a patient's glucose levels stabilize, switching may become an option. High glucose alone is not the determining factor; the concern is whether glucose fluctuates enough to require frequent dose adjustments. Kidney and liver function are additional considerations.

We believe that once-weekly insulin could be an excellent option for an older adult living at home who has difficulty managing daily injections.

A family member or caregiver could assist with the injection once weekly. This approach may reduce the burden on patients, caregivers, and families by decreasing the number of injections and finger sticks required.

Once-weekly insulin may also help people with limited vision or hand dexterity who have difficulty keeping up with daily therapy. It may be useful for people whose travel or work schedules make daily dosing challenging. Other fields, such as psychiatry, have experience with weekly or monthly long-acting injectable medications. A similar model may apply in diabetes care: a patient could come to a clinic once weekly, visit another care setting, or receive help from a nurse, caseworker, family member, or other support person.

Choose your patient and ensure they are the right candidate for the right therapy at the right time.

Jen Pettis:

You've mentioned a couple of safety considerations, including the risk of hypoglycemia. What other safety concerns have trials shown?

Rodolfo Galindo:

One concern people have is what happens if someone accidentally administers a double dose. Novo Nordisk conducted a study in Austria comparing double- or triple-daily insulin dosing with double- or triple-weekly dosing. As expected, additional insulin increased the risk of hypoglycemia, although not all participants experienced it. Recovery from hypoglycemia and the body's response to the weekly double dose were similar to those observed with daily insulin. The study did not identify an additional safety signal from weekly dosing beyond the increased risk expected with additional insulin administration.

These insulins can cause hypoglycemia, and any medication taken in excess can cause adverse effects. Another consideration is how to manage once-weekly insulin when a patient needs surgery, hospitalization, or another procedure. Papers are emerging on patients in the trials who were hospitalized; the available findings suggest they generally did well. Clinicians still need to be more careful because the once-weekly dose remains active when a patient is hospitalized, undergoing a procedure, experiencing kidney failure, not eating, or fasting for a prolonged period. However, the studies did not show that patients remained hypoglycemic for the entire week. That is not being shown anywhere. The way it works is that it doesn't drop you every day. It works a little bit every day for the week. I don't know. This is what we know from the study, but in practice, the experience has been very limited. I think that in one or two years, we're going to have a lot of conversations from real-world experience.

Jen Pettis:

How should clinicians talk with patients about the potential for handling missed doses or dosing errors? What advice would you give your patients about that?

Rodolfo Galindo:

Anyone using intensive insulin therapy should use continuous glucose monitoring when available. If CGM is not available, glucose should be checked more often while insulin is being adjusted. After an accidental double dose, the patient should be monitored closely, and hypoglycemia should be treated using standard measures. One study showed that recovery from hypoglycemia with once-weekly insulin was similar to recovery with daily basal insulin. Patients should follow their clinician's instructions and seek urgent care if glucose levels cannot be kept in a safe range or if symptoms are severe.

They're just going to tell you, look at your sugars. At least, don't be afraid that if they double, they'll be low all week. That did not happen, of course, and the recovery was the same from the regular therapy for hypoglycemia; it's not that you need to do double glucose loading with sugars, drinks, candies when you have a low. The recovery would be similar to what people would do with daily basal insulin.

Jen Pettis:

How about when clinicians are making that decision? You've talked a little bit about either transitioning or that insulin-naïve patient that's starting therapy. What are certain patient characteristics, product-specific information, or any other monitoring you're going through as you're transitioning or beginning that once-weekly dose on someone who has never been on insulin?

Rodolfo Galindo:

With any therapy, you need to find the right patient for insulin. Once you know the patient can take insulin, I guess the conversation turns to what they need. The first step is to determine whether insulin would be a therapy the patient would adhere to. The second step is to determine whether it's weekly, daily, or once a day. I have the impression that the patient will prefer once weekly because it's simpler and less burdensome. Keep in mind that if they are not savvy and want to do it once a day, we have plenty of data on once-a-day insulin. You need to talk to your patient and explain what I was saying. It's no longer the same insulin, but a higher, larger number of units. That's basically practicing as a clinician.

Jen Pettis:

You already mentioned people going into the hospital and doing well, and you've also mentioned other post-acute care settings. What about transitioning between those settings if someone is on this once-weekly insulin? Are there any considerations as they make those care transitions?

Rodolfo Galindo:

Not too much experience. Yes, many studies switched from daily to weekly dosing, essentially multiplying the daily dose by 7 and administering it once weekly. Then adjust it again the following week. That's for people who were in the general outpatient clinic, no issues. If they had surgeries, hospital admissions, procedures, we don't know too much. That area, we're still learning. It's just monitoring glucose more often.

If there is a special situation, prolonged fasting or not able to eat or anything or bowel rest, it's just monitoring the glucose and then using an infusion of dextrose if needed, as we do for many other things.

Jen Pettis:

As we come to an end here, I want to ask you: if you had one key takeaway for your clinician colleagues on caring for older adults with Type 2 diabetes in light of the emergence of once-weekly insulin, what would it be?

Rodolfo Galindo:

For older adults, clinicians are often careful to avoid overly intensive therapy, although undertreatment may not be appropriate either. From an ethical standpoint, age alone should not limit how we treat people. When someone has an advanced condition or another factor that increases the risk of harm, less intensive therapy may be appropriate regardless of age. Treatment decisions should reflect the individual's health status, goals, preferences, and risk of adverse effects, not age alone. If you can have less burden, be free of injections, and have less burden, and your family also has a big burden of care on you because you need help, this will definitely take away six injections a week and do one.

Jen Pettis:

As a nurse who spent her career caring for older adults, many of whom were in post-acute care settings, I appreciate the potential impact on patient safety and the reduction of dosing errors. Once-weekly insulin could be a game-changer for post-acute care. Dr. Galindo, it's always a pleasure to talk with you and hear your expertise and insights. This is an exciting development for people living with diabetes and their families. Today's discussion helped us understand the science and clinical evidence, and it sounds like more evidence and more questions will emerge. Thank you so much for joining me, as always.

Jen Pettis:

To our listeners, thanks so much for joining us for this episode of GSA Momentum Discussions. Dr. Galindo, thanks again.

Rodolfo Galindo:

Excellent. Thank you very much. Always happy to collaborate with your team, Jen. Thank you very much. Thank you.

Announcer:

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