

A Pharmacist's Take: Navigating Diabetes Drug Shortages



PODCAST 36 - Part 1

SOUNDBITE:

Dr. Heather P. Whitley

It goes back to supply and demand where we have had a boost of more patients and providers using the GLP-1s.

00:09

Dr. Jane Caldwell

Welcome to the *On Medical Grounds* podcast, where you can find an authentic, audible blend of timely scientific and medical knowledge. Today *On Medical Grounds*, we will be speaking with Dr. Heather Whitley. Dr. Whitley is a clinical professor in the Department of Pharmacy Practice at the Auburn University Harrison College of Pharmacy. She is a board certified pharmacotherapy specialist and a certified diabetes educator.

Dr. Whitley is well published, predominantly on diabetes-related research. Earlier this year, Dr. Whitley spoke with us about screening for diabetes in high-risk individuals. Today, she is back to talk about some new things going on in the diabetes and pharmacy world.

This is part 1 of a two part series.

Hello, Dr. Whitley. Welcome to *On Medical Grounds*.

Dr. Heather P. Whitley

Thank you so much for having me. It's great to see you again.

01:08

Dr. Jane M. Caldwell

Recently, you co-authored a special report in the journal, *Clinical Diabetes*. It was titled, "Potential Strategies for Addressing GLP-1 and Dual GLP-1/GIP Receptor Agonist Shortages." We'd like to discuss your findings and learn more about how pharmacists and patients can cope with drug shortages. For those, thank you. For those unfamiliar with medical terms, what are GLP-1 and dual GLP-1/GIP receptor agonists, and what are they used for?

Dr. Heather P. Whitley

Sure, well thank you again for having me. It's great to be here and it's a pleasure to be able to share this information, particularly as it relates to the shortages of these important and valuable products for your listeners. First I'll start off by saying that GLP-1 and GIP are hormones that are made in your body. Everyone should make them, they're released from the small intestine and they help regulate blood sugar and then

they also help regulate satiety. So these naturally produced hormones in your body helps with managing those two aspects. And they've since been developed as medications that we can give exogenously. So typically injected to help manage diabetes, mostly type 2 diabetes. And then some of the medications are also FDA approved for managing weight as well.

02:36

Dr. Jane M. Caldwell

Alright, thank you. What are the trade names consumers might recognize for these products?

Dr. Heather P. Whitley

Okay, so for the GLP-1s, and so those are the medications that are just mimicking that one hormone, that's an incretin hormone, there is dulaglutide, which is Trulicity®, there is semaglutide, and that is available as two different forms. One is an injectable form of Ozempic®, the other is an oral formulation, it's the only orally available product of the class called Rybelsus®.

There is exenatide, there's two formulations of that. Byetta® is the twice daily injectable, and then Bydureon® or Bydureon BCise® is the once weekly injectable product. Liraglutide, and that is a once daily injected as Victoza®. That brand is FDA approved for type 2 diabetes, Saxenda®, it's approved for weight loss.

And then tirzepatide, and tirzepatide is a dual, is the only dual GLP-1 GIP, incretin mimetic, and that one is marketed as Mounjaro® for diabetes, and it was just recently FDA approved for weight loss called Zepbound®. And then also back to semaglutide, when it is approved, we're used as a weight loss that is Wegovy®. So we have a handful of different medications, and some of them have dual indications for treating diabetes and then also weight management as well.

04:15

Dr. Jane M. Caldwell

Wow, that was quite a mouthful. For our listeners, I'd like you to know that we will have a slide which summarizes all the different consumer names and what their mode of action is. Your new clinical diabetes special report states that we're experiencing national shortages of these drugs. Can you explain to our listeners why this is happening?

Dr. Heather P. Whitley

Yes, this seemed to emerge around this time last year and where we just people, patients were coming to us in clinic. I work in a family medicine doctor's office to take care of patients that have type 2 and type 1 diabetes. And I had so many patients coming to clinic that were saying they couldn't access the products. We were having a national shortage. And lots of questions were emerging about how to manage this time of lack of access. And so that's where the publication came. I wrote it in collaboration with my co-authors, Joshua Neumiller and Jen Trujillo. And we hope that would be helpful to our clinical colleagues for them to help manage the shortages that they're experiencing. But here we are a year later and we're still having these shortages and we're still having these questions surrounding, well, how do we manage these challenges? It seems like it goes back to supply and demand where we have had a boost of more patients and providers using the GLP-1 and dual GLP-GIP receptor agonist class, which is great. These are fantastic products. They have a handful of benefits that we can provide our patients.

And it's expanded beyond just those with type 2 diabetes to also include patients that are wanting to

facilitate weight loss, which I think that's where that increased demand is coming from. And I honestly believe that we didn't, the manufacturers didn't quite expect the boom that we received and the number of patients and providers that want to utilize these medications and the supply just hasn't been able to meet that demand that we're experiencing.

06:24

Dr. Jane M. Caldwell

Do you think that providers and pharmacies should be able to prioritize those specific prescriptions for patients with diabetes rather than weight loss?

Dr. Heather P. Whitley

That's a tricky question. I think it's an ethical question. In the prescriber hands, we always want to do, and dispensing, we always want to do the best that we can for our patients. We want to provide them the right product for any given patient. And when I'm seeing patients in clinic, I'm not just prescribing one anti-hyperglycemic for my patients, but I'm really thinking about every class and within any particular class, I'm thinking about the individual agents, talking to the patient at hand to identify what the right product is for that patient. That said, with this time of shortage, you do have to kind of jockey a bit and think about, well, what's available, what's not available. Now at the community level, at the dispensing side for the pharmacist, there's going to be a time where you only have so many vials or so many syringes or so many pins of a given GLP-1, but more prescriptions coming in than that.

And that's a tricky situation. I can appreciate from the community side how you want to be able to ideally provide those prescriptions to everybody that has been appropriately given a prescription, but you just don't always have that supply. I think pharmacists should use their discretion when dispensing those to give them to the right patient and the best patient, but they don't always have the objective information to discern severity of disease. For example, they might not have the different A1Cs for a patient with type 2 diabetes, so when that has a very high A1C that's uncontrolled is critical that we bring that blood sugar down to avoid a possible hospital admission versus somebody that is at a better control level. Still, they both need them because they're using that drug therapy to manage it.

And then on the side of obesity or weight management, that's a legitimate chronic disease too. And it has impact on a handful of different complications that can develop from there. So I think it's very hard at that point of the dispensing pharmacist to discern one patient needs it over somebody else. And it does put them in a very tricky position.

08:52

Dr. Jane M. Caldwell

So for patients who can't access their anti-hyperglycemic drugs due to these shortages, what are their alternatives?

Dr. Heather P. Whitley

Yeah, they need to manage their blood sugar. They need to continue to keep it in a reasonable range for risk of precipitating an emergency room visit or complications that can result from that. I think it's very important for them to have open, direct conversation with their healthcare providers, both their pharmacists to say, well, do you know when it might be coming in? Do they have an idea of how long

they might be without and then communicate that back with their health care provider to say, I'm without whatever therapy, this is the last time I took that product or I have five more doses available. So I expect that I'll run out by a certain date. So that the patient and that health care provider can consider all their avenues of how to manage that hyperglycemia during this interval of not having that particular therapy. Good communication and be proactive about it too. Don't wait till you run out and haven't had it for two or three weeks. Be upfront, be aware of how much medication you have available and so that you can get ahead of the problem.

10:11

Dr. Jane M. Caldwell

So what happens to patients with diabetes if they miss just a single dose?

Dr. Heather P. Whitley

Well, it does depend on which GLP-1 they're using. So the rapid acting GLP-1s like Byetta®, which I don't think are taken or used as often, but they will have a postprandial rise pretty quickly within a matter of, so it's a twice daily medication. So in a matter of missing a few days, they're going to have an increase in their after meal blood sugar values.

On the other hand, using some of the medications that are longer acting therapies, particularly the once weekly products, they're going to have, they're going to give a dose one week. They have a whole week until they're going to miss that second dose. Those products have a longer half-life, so a longer duration in the body. So it's going to stick around a bit longer. As soon as they get the product, go ahead and administer it. If they're a few days late on that, a once weekly product, I don't think they're going to see a profound change in their blood sugar, but certainly they are if they miss several weeks at a time.

11:16

Dr. Jane M. Caldwell

So what happens if they miss their doses for an extended period?

Dr. Heather P. Whitley

Their blood sugar will go up. And how high it goes up depends on how much, how controlled their blood sugar is at baseline and how much medication or the dose that they have to use to control it. So for example, if a patient's blood sugar is near goal and they're using the low dose of that GLP-1 to control that, their sugar will certainly bounce up, but I wouldn't say it would necessarily go sky high.

But if they're using a high dose of that GLP-1 to control their blood sugar, and maybe even it's not doing a full job of controlling their blood sugar, maybe they're still a little bit higher at baseline, then it has a much greater risk of it increasing to a point where they absolutely are going to need additional therapy and might need to be more cautious about making sure that they don't flip into one of those concerning diseases of like diabetic ketoacidosis where it's a medical emergency.

12:19

Dr. Jane M. Caldwell

Can you talk more about re-initiating, taking these GLP-1 receptor agonists? Is there a step-wise dosage? How do you do that?

Dr. Heather P. Whitley

Sure. So the most common adverse events that we see from this class of medications is gastrointestinal in nature, predominantly nausea, vomiting. And that happens in about 10 to 20% of people. So not all people, it's just, it's a low, moderate range. But for that reason, when we initiate those therapies, we start at the lowest dose. We always start at the lowest dose to allow their body to get used to that adverse event before increasing the dose. So when we start that dose and we increase, if the patient has been off of it for a while, when the therapy is re-initiated, they might have re-emergent of that nausea, vomiting, tolerability issue. So the question comes into play is if they have been on a consistent use of a higher dose that they have slowly graduated up to, and then they miss a handful of those doses, do we reinitiate all the way at the very starting dose again? Or can we start at that high dose right away and not expect to experience that gastrointestinal intolerance? So that's where the question emerges with the challenges that we're seeing with the shortage.

So, if I can give some guidance about that, talking with the manufacturers to try to find some information which we outline in that article from *Clinical Diabetes*. There's guidelines in the package inserts, but when we evaluate a little bit further, there's a bit more wiggle room. And so for me as a rule of thumb without like looking at the table that's available in that article, I kind of think of a patient has missed two doses or less that they can reinitiate at the dose that they were on. If they missed three to four doses, we can probably start at the step two, like not the very bottom dose, but the second step up in the dosing scale. And then if they've missed five doses or more, then we probably have to initiate all the way back at that starting dose, all for the purposes of avoiding that emergent gastrointestinal challenges.

14:51

Dr. Jane M. Caldwell

That's very useful information. Can you also interchange the different GLP-1 receptor agonists if one product is available while another one isn't? Can they pivot to a different one?

Dr. Heather P. Whitley

Yes, and that has been a technique that I've used a lot in my clinic to help manage these shortages is I will go from if the patient hasn't missed any doses I will go from whatever the dose is of their primary GLP-1 to a glycemic equivalent dose of another GLP-1 so across the board as opposed to you don't have to start all the way down at the starting dose of the second GLP one but more of a glycemic equivalent dose.

15:31

Dr. Jane M. Caldwell

Are there alternative drug types or combinations of drugs which can be used in place of GLP-1s?

Dr. Heather P. Whitley

Yes, so certainly we have a variety of different other pharmacologic options to use when we can't use a GLP-1. And I would say you need to start by considering why you're using the GLP-1 in the first place.

The most common reasons to use the GLP-1 is either for blood sugar control, so that's in type 2 diabetes, for weight management, or for cardio renal benefits, one of those three different reasons, and then selecting your alternative therapy based on that indication. So for example, if we're managing cardio renal benefits, that's why we're using the GLP-1, then the only other class of medications that we could select from is

the SGLT2 inhibitor class. So those are products like Jardiance®, which is empagliflozin, Farxiga®, which is dapagliflozin, or Invokana®, which is canagliflozin. And there's a few other products in the class too, but those are the three that have been proven to have some of those cardio renal benefits. If we are using the GLP-1 receptor agonist for weight reduction, likewise that SGLT2 inhibitor class is the only other class that has proven benefit to facilitate weight loss. And of course there's a collection of other products that we can use for managing weight outside of these anti-hyperglycemic classes. And then in type 2 diabetes, if we're only just trying to manage their blood sugar, we just pick another product, another anti-hyperglycemic that all have those benefits while considering what their side effect profile is, what might work best in our given patient.

17:16

Dr. Jane M. Caldwell

It's nice to know that there are alternatives that patients can consider. Some patients are sourcing their own medications online because they can't get them at the pharmacy. What are some of the dangers of online sources of these particular drugs?

Dr. Heather P. Whitley

That is not ideal and certainly I will say that through this time of managing the shortages that we have seen with the GLP-1s, no alternative is the ideal alternative. And so we're trying to identify other avenues that we can move towards to help continue to maintain the therapeutic goal that we're working to achieve with the GLP-1. Online sources are tricky because you don't always have that clear patient provider relationship in my opinion. I think that when you're dealing with a provider online, sometimes there's a lack of just miscommunication that can happen through the telephone or text message or email, beyond even video. If the product is not manufactured in the United States, which is common, but it's also not under good manufacturing procedures, you have risk of having more contaminants or even getting a product that isn't what it's sold to be. And so I think as the user, you have to be very savvy and thoughtful about where you're getting those products, where those products are coming from to make sure that you are in fact getting what you're purchasing.

18:50

Dr. Jane M. Caldwell

What about compounded products?

Dr. Heather P. Whitley

We have seen a tremendous boom in the utilization of compounded GLP-1s during this shortage for several different reasons. One is it's a protein, a big bulky protein, which we cannot easily manufacture in the lab, but FDA is reasonable to compound when it is under short supply. And we've had so many people wanting to use these products, particularly for weight loss. And so they are looking to gain access through different means if they're not able to get them directly from the typical dispensing pharmacy to get the manufacturer's variety of that product. So we have these compounding pharmacies that are producing these products. But I pause because if the product is in short supply where the pharmacies getting these products to make, to compound the product in the first place. So I am curious if that's probably not the product is not coming from the manufacturer themselves.

So we are seeing increased manufacturing compounding products of different salt formulations of the products. So for example, in the manufacturer of Ozempic® or Wegovy®, semaglutide, we're seeing

compounded products of a salt formulation like semaglutide sodium or semaglutide acetate. That is not the version that was studied in all of the different clinical trials to bring the product to market that demonstrated not only efficacy, but safety. So there's some unknowns in that area. Whereas a clinician, I cannot tell a patient that with certainty, we know it will have the same benefit or even the same safety profile of what was studied. There have been reports to the FDA of some adverse events that have occurred with using the compounded products that has not been openly disclosed. I've heard a conversation that it just simply increased in blood pressure. And certainly we know that high blood pressure is a silent killer because of its increased risk of causing heart attack and stroke when it is very high. And so if we're adding a lot of salt into it, that's in a compounded product, that salt is known to increase blood pressure. So I think there's a risk there.

Although I'm just not in a fully educated position to be able to say, well, how much salt is in those compounded products, if that is how it is compounded to be able to determine the full risk. So there's a lot of unknowns currently in the area of compounded products. So I recommend great caution to people when they are deciding to utilize those therapies that are compounded.

21:51

Dr. Jane M. Caldwell

How do you personally manage your patient's expectations and concerns?

Dr. Heather P. Whitley

I work with my patients to have clear and open dialogue so they appreciate the reason for why we're initiating the GLP-1 and what our ultimate goal is. Sometimes that is for the purpose of managing blood sugar, sometimes it's for weight loss, sometimes it's for redesigning their therapeutic regimen that will give them an overall improved quality of life because of a decreased medication-related burden.

And sometimes it's for those cardiorenal benefits. So I make sure that they understand the reason why we're implementing this therapy. I tell them about risks. I tell them that the most common adverse event is gastrointestinal. It's typically nausea, possibly some vomiting. It only happens in about 10 to 20% of people. Typically when we talk about the most common side effect, they think that means everybody or nearly everybody gets it, but that's not the case. And so I make sure I'm clear that it's only about two and 10 people that experiencing nausea in the first place. I let them know that upfront. So when it emerges, they can have some ideas about how to manage it. I remind them that nausea is typically mild to moderate in intensity, and it does go away with continued use.

So that encourages them to stick with the therapy. And then I remind them of things that they can do to help reduce that risk. So typically when we sit down to eat, we have a perspective of how much food we need to put on our plate to fill our stomachs. And with the GLP-1s, one of the ways it works is to improve satiety so that we feel fuller faster. And so it's important for patients to know that they're not going to be able to eat that same volume of food that they did before starting the GLP-1. So I might tell them to fill half of your plate instead of a full plate. Eat slowly. And when you start feeling full, push back from the table. Wait a minute. Assess whether you want some more food or not.

And if you feel full, go ahead, wrap up that plate, put it in the refrigerator and come back to it later on because that GLP-1 making you feel fuller, if they continue to eat, that is when that nausea will most likely

emerge. Typically, patients really appreciate having those anticipatory recommendations that they know how to mitigate those adverse events. One other thing I tell them is that these medications do not typically work fast. So the injection or the dose that they take today is not going to dramatically improve their blood sugar tomorrow or the next day, but rather it takes some time to build up in their bodies. That way if they're managing and they're watching their blood sugar or they're watching their weight, they know it's not an overnight miracle that it does take some time to achieve those results that they're wanting and that helps them stick with it as well.

Dr. Jane Caldwell

Dr. Whitley had much more to say about drug shortages. Tune in to part 2 of this series where we discuss pharmacy deserts and the pharmacist's role in patient care.

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