***Podcast Title:***

**Helping your Clients/Patients Meet their Targets with GLP-1 and GIP/GLP-1 Receptor Agonists**

***Transcript of Recording***

00;00;06;03 - 00;00;38;04

Speaker: Jodi Lavin-Thompkins

Hello and welcome to ADCES podcast, “The Huddle: Conversations with the Diabetes Care Team”. In each episode, we speak with guests across the diabetes care space to bring you perspectives, issues and updates that elevate your role, inform your practice, and ignite your passion. I'm your host, Jodie Lavin Thompkins, a board certified nurse in Advanced Diabetes Management and the director of accreditation and content development at the Association of Diabetes Care and Education Specialists.

00;00;38;19 - 00;01;16;12

Speaker: Jodi Lavin-Thompkins

Our guest today is Christy Schumacher. Christy is a professor of pharmacy practice and director of the PGY2 ambulatory care residency program at Midwestern University College of Pharmacy at the Downers Grove Campus, and a clinical pharmacist at Advocate Medical Group Southeast Center in Chicago, Illinois. She currently works in a primary care clinic to provide comprehensive medication management for a variety of internal medicine disease states, including, but not limited to heart failure, diabetes, hypertension, hyperlipidemia, COPD and asthma.

00;01;16;19 - 00;01;36;27

Speaker: Jodi Lavin-Thompkins

Christy is here with us today to talk about the GLP-1 and GIP/GLP-1 receptor agonists, which are among a class of anti hyperglycemic medications that has been available in the U.S. for 17 years. Support for this episode has been provided by Lilly. IChristy, welcome to The Huddle.

00;01;37;11 - 00;01;44;06

Speaker: Christie Shumacher

Thanks for having me, Jodie. Happy to be here to discuss GLP-1 and GIP/GLP receptor agonists today.

00;01;44;19 - 00;01;51;27

Speaker: Jodi Lavin-Thompkins

So I'm wondering if you can give our audience an overview of these agents and discuss what is currently available.

00;01;52;14 - 00;02;19;15

Speaker: Christie Shumacher

Of course. So these agents have been on the market a while now. However, with the new cardiovascular outcome trials and different data that we've collected through clinical trials, we found a variety of different benefits of using these agents in people with diabetes. So now they're actually indicated and people with atherosclerotic cardiovascular disease or ASCVD or those with indicators of high risk, those with chronic kidney disease or heart failure after SGLT2 inhibitors.

00;02;19;24 - 00;02;44;22

Speaker: Christie Shumacher

And in those that need further glycemic management, as they've been proven to be very efficacious in having persons with diabetes achieve their glycemic management as well as weight management goals. So overall, they've really been quite efficacious, very helpful in helping us manage people with diabetes. And we've actually found that now we can use less insulin and have better outcomes by incorporating these agents into our clinical practice.

00;02;45;06 - 00;03;06;25

Speaker: Christie Shumacher

So out of the GLP-1 and GIP/GLP-1 receptor agents that are available, we have different options. We've got injectables versus orals, and then we have daily and weekly agents. So we have exenatide, which is used twice daily, 0 to 60 minutes before breakfast and dinner. We have liraglutide and lixisenatide and then oral semaglutide which are all once daily.

00;03;07;09 - 00;03;28;00

Speaker: Christie Shumacher

And then we have semaglutide, dulaglutide, exenatide ER as well as tirzepatide, which are all once weekly. There's a variety of agents and it depends really what the person with diabetes is looking for. Is it easier for them to remember to take a medication once a day? They have a pill formulation now with oral semaglutide if a person's hesitant about injectables.

00;03;28;11 - 00;03;57;06

Speaker: Christie Shumacher

And then for those that are looking for just once weekly, we have four options as well now that are for once weekly dosing. There's also indications for cardiovascular risk reduction with dulaglutide, semaglutide and liraglutide, and those were found by looking at the cardiovascular outcomes trials. All three of those agents assess the three point MACE non-fatal MI, non-fatal stroke and cardiovascular death, and they all demonstrated clinical benefit in their respective cardiovascular outcomes trials.

00;03;58;03 - 00;04;12;17

Speaker: Christie Shumacher

So thinking about how these agents work, exenatide, liraglutide, lixisenatide, semaglutide and dulaglutide all work at the GLP-1 receptor. And then now we have tirzepatide which acts on both the GIP and GLP-1 receptors.

00;04;12;29 - 00;04;29;03

Speaker: Jodi Lavin-Thompkins

Yes, it certainly is nice to have these in the toolbox. We need all the help we can get to help people reach their goals. So can you tell us more about the two incretins and their physiologic action in the body, GIP and GLP-1 receptors?

00;04;29;17 - 00;04;51;19

Speaker: Christie Shumacher

Sure. So in persons without type two diabetes, the majority of insulin release after meal is mediated by incretins and these incretins are GIP and GLP-1. However, the effect of these incretins are impaired or slightly reduced in people with type two diabetes. So therefore we want to supplement back GLP-1 and GIP in people with type two diabetes.

00;04;52;08 - 00;05;23;14

Speaker: Christie Shumacher

So in humans, GLP-1 receptor agonism is thought to increase insulin when the blood glucose is high. It's also known to decrease food intake by slowing down gastric emptying, and it also decreases glucagon when the blood glucose is high as well. And then for the GLP-1 receptor agonist, that have cardiovascular risk reduction indications, there's some thought that not all the benefit is attributed to the blood glucose lowering alone, and some evidence suggests that there may be direct effects of GLP-1 receptor agonist on the cardiovascular system.

00;05;24;04 - 00;05;49;25

Speaker: Christie Shumacher

So unlike for GLP-1 receptor activation, there isn't a medication on the market that only targets the GIP receptor. So the actions of GIP receptor antagonism can only be inferred by experimental approaches using experimental compounds. But that being said, glucose dependent insulinotropic peptide or GIP exerts the following actions, some of which have been demonstrated in pre-clinical trials, and some have not been confirmed yet in humans.

00;05;49;25 - 00;06;17;01

Speaker: Christie Shumacher

But this is what's been postulated. So GIP increases insulin when blood glucose is high. It also potentially increases glucagon when blood glucose is low. So it may prevent people with diabetes or just people in general from going hypoglycemic. And contrary to GLP-1 receptor agonists which are believed to induce nausea, GIP might have an antiaversive action and might mitigate some of that nausea.

00;06;17;17 - 00;06;31;19

Speaker: Christie Shumacher

GIP also may decrease food intake in some preclinical models, it's been shown, and it also may improve insulin sensitivity and improve proper storage of triglycerides and use in adipose tissue as opposed to liver and other organs.

00;06;31;29 - 00;06;58;19

Speaker: Jodi Lavin-Thompkins

Christy, thanks so much for that overview of the physiologic action. There's a lot to that. I want to move on to talk about guidelines now. And the ADA and EASD just released their updated consensus report on the management of hyperglycemia in type two diabetes. So could you help us see where these therapies fit into that treatment algorithm that they released?

00;06;58;29 - 00;07;22;23

Speaker: Christie Shumacher

So thinking about the guidelines we're all familiar with the ADA Standards of Care and the new EASD/ADA Consensus Report still is very similar on the left side of the algorithm and that those with clinical ASCVD or those with indicators of high risk. We still want to select the GLP-1 receptor agonist with proven cardiovascular disease benefit. So specifically semaglutide dulaglutide and liraglutide.

00;07;23;08 - 00;07;48;13

Speaker: Christie Shumacher

So we could select one of those agents still on the left side of the algorithm. And then for those with heart failure and CKD, SGLT2 inhibitors are preferred. However, we should still be selecting a GLP-1 receptor agonist with proven cardiovascular disease benefit. If the SGLT2 inhibitor is not tolerated, or if it's contraindicated, or if the A1C is still above target and people with diabetes need additional cardiovascular risk reduction.

00;07;49;02 - 00;08;18;21

Speaker: Christie Shumacher

What's new is the right side of the algorithm. Where now there's a larger focus on glycemic management, as well as meeting and maintaining weight management goals. And this is really where we're starting to see more preference towards the GLP-1 receptor agonist. So when we're thinking about glycemic management, the algorithm really now focuses us or encourages us to think about including metformin, of course, but then an agent such as a GLP-1 receptor agonist with efficacy to achieve or maintain treatment goals.

00;08;19;01 - 00;08;46;26

Speaker: Christie Shumacher

And of course, we want to avoid agents that might lead a person with diabetes to more often has hypoglycemia. So in general, the algorithm now recommends higher efficacy approaches so that the person with diabetes is more likely to achieve their glycemic goals. So now they start to strategize based on very high and high efficacy and intermediate agents. So very high efficacy agents are dulaglutide at high dose, semaglutide and tirzepatide.

00;08;47;05 - 00;09;17;04

Speaker: Christie Shumacher

So now preference is given to those three agents as very high efficacy agents to help people with diabetes meet their glycemic management goals. And then thinking about weight management goals as well. It's still recommending general lifestyle advice and then thinking about encouraging our people with diabetes to enter into a weight management program. But then it considers encouraging people with diabetes to choose glucose lowering therapies that have high to very high glucose and weight efficacy properties.

00;09;17;14 - 00;09;44;24

Speaker: Christie Shumacher

And now they stratify it based on very high, high, intermediate and neutral. So for efficacy for weight loss, very high efficacy, for weight loss now is preferenced as semaglutide and tirzepatide and then high efficacy for weight loss being dulaglutide and liraglutide. So now what we're seeing is GLP-1 receptor agonist and the new GIP/GLP-1 receptor agonist being preferentiated as high efficacy for weight loss as well as high efficacy for glycemic management.

00;09;45;05 - 00;10;03;15

Speaker: Christie Shumacher

So really starting to give preference towards taking more efficacious agents as well as thinking about helping people with type two diabetes meet their weight management goals. And we know that GLP-1 receptor agonists and GIP/GLP-1 receptor agonists can really help our patients or help people with type two diabetes meet their goals.

00;10;04;00 - 00;10;21;15

Speaker: Jodi Lavin-Thompkins

Thank you, Christy. So we know that many people with type two diabetes are on more than one medication for their diabetes. So what is your recommendation for concomitant medication use when starting a GLP-1 and GIP/GLP-1 receptor agonist?

00;10;22;02 - 00;10;55;06

Speaker: Christie Shumacher

Yeah. So for people with type two diabetes now the guidelines really do recommend that we start people on a GLP-1 or GIP/GLP-1 receptor agonist even before insulin to help them meet their glycaemic management goals. However, if a person with diabetes comes into our practice and they're already on maybe insulin or a DPP4 inhibitor or sulfonylurea, one of the things that we do is we start them on a GLP-1 or GIP/GLP-1 receptor agonist, and then we'll want to go ahead and start to taper off potentially the insulin or the sulfonylurea.

00;10;55;27 - 00;11;19;29

Speaker: Christie Shumacher

We usually leave on metformin, the SGLT2 inhibitor if that's already on board. However, our goal is to reduce the hypoglycemic potential and reduce concomitant insulin use and really try to derive full benefit and get up to target or maximum dose of the GLP-1 or GIP/GLP-1 receptor agonist. So what we'll do is usually we first start by de-escalating insulin therapy.

00;11;20;12 - 00;11;41;13

Speaker: Christie Shumacher

So for people that we're starting on a GLP-1 or GIP/GLP-1 receptor agonist, I might decrease the bolus insulin by 20% or even the basal insulin by 20% if they're on a sulfonylurea, let's say glipizide ten twice a day. I'll cut the dose in half when starting a GLP-1 receptor agonist or a GLP-1 receptor agonist.

00;11;41;24 - 00;12;05;07

Speaker: Christie Shumacher

Really trying to remove those hypo agents that have hypoglycemia, potential that really don't have any proven cardiovascular benefit and try to optimize these agents to help with glycaemic management and weight loss. So I would definitely recommend de-escalating and removing insulin therapy as you're adding these agents on as possible. We've actually found that we've been able to take off bolus insulin when we started these agents because they do help curb appetite.

00;12;05;07 - 00;12;30;09

Speaker: Christie Shumacher

They reduce and slow down gastric emptying and people with diabetes are eating less. They don't require as much insulin. And we've been able to remove mealtime insulin therapy for people with type two diabetes, just adding on these agents and titrating up to maximum tolerated dose. If a person with type two diabetes is already on a DPP4 inhibitor.

00;12;30;17 - 00;12;54;22

Speaker: Christie Shumacher

We know that these agents aren’t synergistic and it's really a very similar mechanism of action except the GLP-1 or the GIP/GLP-1 receptor agonist has a much higher efficacy. So to prevent the person with diabetes paying for two brand name copays, we usually just stop the DPP4 inhibitor upon starting one of these agents just due to the overlapping mechanism of action and considerations for polypharmacy.

00;12;54;28 - 00;13;12;18

Speaker: Jodi Lavin-Thompkins

Those are all really important points you make, Christie. And I know that any time we go to start a new medication, we need to be able to review the side effects for the therapy. And so can you let our audience know what the most common side effects for these therapies are?

00;13;12;25 - 00;13;40;20

Speaker: Christie Shumacher

Sure. I think the most common that we see in clinical practice are nausea, vomiting and diarrhea. And among those that do experience these, they're usually mild to moderate in severity, and they typically occur when the person with diabetes first starts the medication. However, we do notice that they go away over time. So across the GLP-1 and GIP/GLP-1 receptor agonist, the number of people that experience nausea, vomiting and diarrhea varies, meaning some people may experience these side effects and some people may not.

00;13;41;01 - 00;13;56;02

Speaker: Christie Shumacher

Another thing that we've noticed is that some people may have side effects to one medication in the class, and then we'll switch them over to another medication and they may tolerate it very well. So it's very patient specific and really just depends on the patient and how well the agent agrees with their system.

00;13;56;25 - 00;14;12;04

Speaker: Jodi Lavin-Thompkins

Right. So it comes down to individualization again. So, Christie, our audience is probably interested in what your experiences have been with initiating these agents and how you help mitigate the side effects and encourage persistence with the medications.

00;14;12;19 - 00;14;37;10

Speaker: Christie Shumacher

So usually when we counsel people with diabetes about starting a GLP-1 or GIP/GLP-1 receptor agonist, the first thing we want to counsel them on is to get ready to eat less, because we know that these agents slow down, stomach emptying and they help them feel more full. So it's important to counsel people with diabetes to eat smaller sized meals, to eat more slowly and really to stop eating at the first sign of fullness.

00;14;37;18 - 00;14;56;13

Speaker: Christie Shumacher

That's really going to help mitigate some of this nausea and then potentially vomiting if that develops. Another important counseling point is that the person with diabetes may start to notice that they feel a little bit more nauseous, but usually that's going to be mild and resolved within the first couple of weeks if they're eating slowly and stopping at the first sign of fullness.

00;14;56;29 - 00;15;20;12

Speaker: Christie Shumacher

If they continue to have issues, it's good to recommend low fat foods. It's also good to start at the lowest dose of this agent of the GLP/GIP, or GLP-1 receptor agonist and titrate slowly based on the prescribing information. And if the side effects do develop, just have them mention to their physician or provider and they could possibly decrease the dose back to the highest tolerated dose.

00;15;20;25 - 00;15;36;16

Speaker: Christie Shumacher

So overall, I think the most important counseling point is really preparing the person with diabetes that they have to be ready to eat smaller, more frequent meals and then just stop eating at the first sign of fullness. And that should really help hopefully prevent some of the nausea that they might experience with these agents.

00;15;36;28 - 00;15;45;02

Speaker: Jodi Lavin-Thompkins

So now we know what some of the side effects are and how to mitigate them. But what is the actual prevalence of the side effects?

00;15;45;14 - 00;16;05;03

Speaker: Christie Shumacher

Sure. So nausea usually occurs in about one in five or 20% of people with diabetes. Vomiting, 13%. And in diarrhea, maybe about 17%. Now, these are all the possible side effects that patients may complain about. They may also complain of decrease appetite, abdominal pain from these agents, among others.

00;16;05;15 - 00;16;11;01

Speaker: Jodi Lavin-Thompkins

All right. At what point do the nausea, vomiting and diarrhea become a safety concern?

00;16;11;10 - 00;16;35;28

Speaker: Christie Shumacher

All right. So we have to be careful with these agents and those with gastroparesis or other GI issues. In addition, we want to monitor for adverse GI reactions that may cause volume depletion in those with acute or chronic kidney disease. So it's important to keep an eye out for that. Also keeping in mind that, exenatide IR and ER as well as lixisenatide have dosing cutoffs in kidney disease.

00;16;36;09 - 00;16;52;28

Speaker: Christie Shumacher

So just be aware that those three do have kidney dosing adjustments. If the side effects become bothersome or don't go away definitely counsel the person with diabetes to reach out to their provider because sometimes therapies need to be discontinued and another agent may be more appropriate.

00;16;53;12 - 00;17;03;06

Speaker: Jodi Lavin-Thompkins

Well, Christy, you've given us a lot of great information, a nice overview of using these agents. Do you have any other consideration since you want to leave our listeners with?

00;17;03;17 - 00;17;28;02

Speaker: Christie Shumacher

Yeah. So in general, these are very efficacious agents. We don't use as much insulin in our practice anymore. Now that we have these available and we've seen much better glycemic management as well as weight management since we started incorporating these regularly into our clinical practice. In addition, we know from the cardiovascular outcomes trials that liraglutide, semaglutide and dulaglutide have additional cardiovascular disease benefit.

00;17;28;10 - 00;17;52;06

Speaker: Christie Shumacher

So overall, we're getting cardiovascular risk reduction, weight management, we're seeing less insulin use and really they're just overall great for our patients. We've had a lot of success with people with weight loss just feeling better about themselves, really kind of motivating them to start taking better care of themselves, start exercising more, eating better. So with proper counseling, we can see really great results with these agents.

00;17;52;16 - 00;18;02;13

Speaker: Christie Shumacher

It's so nice to see an agent with great efficacy in such a low risk hypoglycemia when used on its own. Overall, these are definitely preferentiated in our clinical practice.

00;18;03;02 - 00;18;22;16

Speaker: Jodi Lavin-Thompkins

Christy, thank you so much for taking the time to join us for this episode of The Huddle and for sharing your knowledge and experience with our audience. For me, as a diabetes care and education specialist, I know how useful this information is for practice. So I'm sure our listeners really appreciate hearing your firsthand experience.

00;18;22;28 - 00;18;25;00

Speaker: Christie Shumacher

Thank you, Jodie. It was great to be here today.

00;18;25;10 - 00;18;52;12

Speaker: Jodi Lavin-Thompkins

Thank you for listening to this week's episode of The Huddle. To access the notes and resources from today's episode, head over to diabetes educator dot org forward slash podcast. And remember ADCES membership gets you free access to resources, education and networking. That improve your practice and optimize outcomes for your clients. Learn more about what ADCES can do for you.

00;18;52;19 - 00;19;20;12

Speaker: Jodi Lavin-Thompkins

At Diabetes Educator dot org forward slash join. This episode was sponsored by Lilly, a global leader in Diabetes Care since 1923. The information presented here is for informational purposes only and may not be appropriate or applicable for your individual circumstances. This podcast does not provide medical or professional advice and is not a substitute for consultation with a health care professional.

00;19;20;28 - 00;19;32;08

Speaker: Jodi Lavin-Thompkins

Please consult your health care professional for any medical questions.