PharmaNote
Vol. 32, Issue 8 May 2017 Established 1985

Lixisenatide (Adlyxin®): A New GLP-1 Agonist For Type 2 Diabetes Mellitus

Farris Hasan, PharmD Candidate

Diabetes mellitus is a disease that affects over 29 million people in the United States.[1] Uncontrolled diabetes can lead to both microvascular and macrovascular complications including but not limited to nephropathy, neuropathy, coronary artery disease, peripheral vascular disease, and stroke. Treatment of diabetes can incorporate both lifestyle modifications and pharmacotherapy. The American Association of Clinical Endocrinologists (AACE) and the American Diabetes Association (ADA) recommend metformin as the first line option for patients with type 2 diabetes. Patients with uncontrolled glycemic values even after metformin initiation are encouraged to add on another diabetic agent to treat hyperglycemia.[2,3] The addition of other diabetic medications is primarily based on patient factors, side effect profile, and cost. Recently, there has been an increasing amount of knowledge about glucagon-like peptide-1 (GLP-1) agonists and their role in type 2 diabetes mellitus. On July 28th, 2016, the FDA approved the newest medication in the GLP-1 class called lixisenatide (Adlyxin®). Lixisenatide is a once daily injection indicated for the treatment of type 2 diabetes in combination of oral glucose lowering agents and/or basal insulin to help achieve glycemic control. The purpose of this article is to review lixisenatide in the treatment of type 2 diabetes, including a review of pharmacology, pharmacokinetics, clinical trials, brief comparison between other medications in the same class, adverse effects, dosing, interactions, and costs.

Clinical Pharmacology

Lixisenatide activates the GLP-1 receptor, thereby mimicking the incretin effects in the body. Incretin consists of two major natural hormones, GLP-1 and gastric inhibitory polypeptide (GIP), which reside in the gut and are released upon ingestion of carbohydrates or fats in order to regulate glucose homeostasis. These incretin hormones are responsible for increasing insulin from beta cells in the presence of elevated glucose, increasing glucose uptake by muscles, decreasing glucagon secretion, slowing gastric emptying, and increasing satiety. Patients diagnosed with type 2 diabetes tend to have a loss of the incretin effect over time due to the reduced amount of the GLP-1 hormone and an increased amount of dipeptidyl peptidase-4 (DPP-4), which is an enzyme that breaks down both GLP-1 and GIP.[4]

Pharmacokinetics

Lixisenatide is a 44-chain amino acid peptide structurally similar to exendin-4 (the main amino acid chain responsible for exenatide) with the exception of 1 less proline group and an additional six-lysine residue group attached at the C terminal of the peptide structure. Due to these slight modifications on the exendin-4 structure, lixisenatide has an ability to delay gastric emptying and attenuate postprandial glucose excursions without causing desensitization of this effect after repeated use.[5] Lixisenatide has a median t-max, or time it takes to reach maximum plasma concentration of 1-3.5 hours with no differences in absorption when administered at disparate subcutaneous sites in the body (i.e. abdomen, thigh, or arm). The injection is mainly eliminated in the kidneys with a terminal half-life of approximately 3 hours.[6] These properties allow for a once a day injection regimen.

Clinical Trials

There have been eleven phase III clinical trials both evaluating lixisenatide safety and efficacy while also defining its role in diabetes management. These eleven randomized trials are also known as the GetGoal Program. In the clinical trials, lixisenatide was evaluated as monotherapy as well as with other common diabetic medications. This article will focus on 6 of the 11 GetGoal trials: GetGoal-Mono, GetGoal-M, GetGoal-S, GetGoal-P, GetGoal-L, and GetGoal-X. These trials were selected due to the generalizability of the study (multinational, multicenter), the population size, study design (randomized, placebo controlled, double blind trial), the varying degree of ethnic groups involved, and their ability to match lixisenatide with other common diabetic agents to compare with placebo. GetGoal-X was selected to compare lixisenatide to an established GLP-1 agonist, exenatide. A summary of the clinical trials discussed is provided in **Table 1**.

GetGoal—Mono

GetGoal-Mono was a randomized, multinational, placebo controlled, double blind trial that included 361 patients with type 2 diabetes attempting to control their hyperglycemia with diet and exercise alone.[7] The primary endpoint of the study was to evaluate the A1c change from baseline to week 12. Patients were included in the study if they were within the age of 20 to 85 years old, were not on glucose lowering agents, and had a baseline A1c value be-

Table 1 | Summary of Select GetGoal Trials.[5,7-12]

Trial	Patient (n)	Intervention	Additional Treatment	Duration (weeks)	Baseline A1c (%)	Δ A1c (%)	A1c<7% (%)	P-value[a]
GetGoal-Mono	361	Lix 20 mcg (1 step) Lix 20 mcg (2 step) PLBO	------	12	8.1 8.1 8.0	-0.94 -0.77 -0.2	47 52 27	P<0.01
GetGoal-M	680	Lix 20 mcg am Lix 20 mcg pm PLBO (AM & PM)	Met	24	8.0 8.1 8.1	-0.9 -0.8 -0.4	43 40.6 22	P<0.0001
GetGoal-S	859	Lix 20 mcg QD PLBO	SU ± Met	24	8.3 8.2	-0.9 -0.1	36.4 13.5	P<0.0001
GetGoal-P	484	Lix 20 mcg QD PLBO	Pio ± Met	24	8.1 8.1	-0.9 -0.3	52.3 26.4	P<0.0001
GetGoal-L	496	Lix 20 mcg QD PLBO	Insulin ± Met	24	8.4 8.4	-0.7 -0.4	28.3 12	P<0.0001
GetGoal-X	634	Lix 20 mcg QD Exe 10 mcg BID	Met	24	8.0 8.0	-0.8 -1.0	48.5 49.8	Not reported

[a]change in A1c with active treatment(s) vs placebo.
Exe = exenatide; **Lix** = lixisenatide; **Met** = metformin; **Pio** = pioglitazone; **PLBO** = placebo; **SU** = sulfonylurea

tween 7-10%. Mean duration of diabetes among each of the three groups ranged from 1.1 to 1.4 years. The treatment arms included lixisenatide daily injection as a one step and two step titration to maintenance dose compared to placebo. Baseline average A1c was 8.07%, 8.07%, and 7.98% in the placebo, one step lixisenatide, and two step lixisenatide comparison groups, respectively. Participants in the one step titration group were initiated with a 10 mcg injection for 2 weeks and transitioned to 20 mcg starting on day 15. Participants in the two step titration group were initiated with 10 mcg for week 1, 15 mcg for week 2, and 20 mcg at day 15. The goal A1c < 7% was successfully obtained by 52% of patients in the two step lixisenatide group, 47% in the one step lixisenatide group, and 27% in placebo (p<0.01). Interestingly, the one step titration regimen had a greater reduction in A1c compared to the two-step titration regimen (0.66% vs. 0.54%, p<0.0001).[7] A subgroup analysis was conducted within the trial which included 169 patients and measured the 2-hour post prandial glucose (PPG) and 2 hr plasma glucose excursion after the administration of lixisenatide and placebo. Lixisenatide reduced PPG by roughly 81 to 99 mg/dl, compared to a 12.6 mg/dl reduction with placebo.[7] Although the one step and two step titration scheme were well tolerated throughout the study, the most common side effects included gastrointestinal (GI) issues (i.e., nausea, vomiting, and diarrhea). This study showed that lixisenatide is a safe and effective medication that can reduce both PPG and overall A1c with patients who have uncontrolled diabetes on diet and exercise alone.[5,7]

GetGoal—M

GetGoal-M was randomized, multicenter, multinational, placebo controlled, double blind trial that included 510 patients with type 2 diabetes. The purpose of the trial was to evaluate the efficacy and safety of morning or evening lixisenatide dose titrated up to 20 mcg compared to placebo for patients inadequately controlled on metformin alone. The trial included patients on an average metformin dose of 2000 mg daily and a mean duration of diabetes of 5.9 to 6.2 years. Baseline A1c average between the groups were 8.0%, 8.1%, and 8.1% for the lixisenatide morning, lixisenatide evening, and placebo groups, respectively. Participants were randomized to 4 different treatment arms: lixisenatide once daily injection < 1 hour prior to morning meal, placebo in the morning, lixisenatide once daily injection < 1 hour prior to evening meal, and placebo in the evening. Both lixisenatide morning injection compared to morning placebo and lixisenatide evening injection compared to evening placebo significantly improved glycemic control with a mean decrease in A1c of 0.5% and 0.4% respectively (p<0.0001). The proportion of patients reaching a target A1c of < 7% was 43% in lixisenatide morning injection, 40.6% in lixisenatide in the evening, and 22% for the combined placebo groups (p<0.0001). Additionally, both Lixisenatide groups reduced 2 hour PPG and glucose excursion by 81 mg/dl and 70.2 mg/dl, respectively.[8] GI side effects were similar in both the lixisenatide morning (22.7%) and lixisenatide evening (21.2%) groups; however, they were found to be greater compared to placebo (9.4% for the placebo morning group, and 13.3% for the placebo evening group). Symptomatic hypoglycemia was more prevalent in the evening dose at 5.1% compared to just 2.4% for the morning dose.[8] This study demonstrated that lixisenatide 20 mcg once daily injection (morning or evening) improved glycemic control in those patients concurrently taking metformin.

GetGoal—S

Just like the previous two trials, GetGoal-S was a multicenter, multinational, double blind, randomized, placebo controlled trial consisting of 859 patients inadequately controlled on a sulfonylurea ± metformin (about 84% of patients were on metformin). The most common sulfonylureas were glimepiride and glyburide with a mean dose of 5.1 mg and 12.9 mg, respectively. Patients were either administered lixisenatide 20 mcg once daily injection or placebo for 24 weeks. Baseline characteristics for the participants were approximately equal among groups with an A1c value at baseline of 8.3% for the lixisenatide group and 8.2% for the placebo group. Combining lixisenatide with a sulfonylurea ± metformin significantly reduced A1c compared to placebo with a mean reduction in A1c of 0.85% compared to just 0.1% reduction with placebo (p<0.0001) at 24 weeks. The percentage of patients achieving an A1c of < 7% was 36.4% for the lixisenatide group and 13.5% for placebo (p<0.0001). Patients reaching a goal A1c < 6.5% in the lixisenatide group was 19.3% compared to just 4.7% in placebo (p<0.0001). Furthermore, lixisenatide added to this

group of patients also had a statistically significant reduction in 2 hour PPG with a mean change of 6.2 mg/dl compared to 0.2 mg/dl with placebo (p<0.0001). Similar to the previous trials, the most common side effects associated with lixisenatide use included nausea, vomiting, and diarrhea, which were higher in the treatment group compared to placebo (40.9% vs. 20%). Symptomatic hypoglycemia was also documented as 15.3% for the lixisenatide group and 12.3% for the placebo group.[9] Based off of the GetGoal-S trial, the addition of lixisenatide to patients inadequately controlled on a sulfonylurea ± metformin had a significant improvement in glycemic control without a significant increase in side effects.

GetGoal—P

GetGoal-P was another randomized, double blind, placebo controlled, parallel, multicenter, multinational trial comprised of 484 patients inadequately controlled on pioglitazone (>30 mg) ± metformin (81% patients). Of the patients taking pioglitazone, 75% were taking 30 to 45 mg daily in the lixisenatide group compared to 78.3% in the placebo group. Participants were randomized to either a two-step titration regimen of lixisenatide 20 mcg daily or placebo. Baseline A1c for both groups were 8.1%. The addition of lixisenatide significantly reduced baseline A1c over the span of 24 weeks by -0.9% while the placebo group reduced baseline A1c by -0.34% (p<0.0001). The percent of patients reaching a goal A1c of < 7% was 52.3% in the lixisenatide group compared to 26.4% in the placebo group (p<0.0001). The amount of patients that were able to reach a goal A1c < 6.5% was 28.9% in the lixisenatide group versus 10.1% in the placebo group (p<0.0001). Body weight was slightly reduced in the lixisenatide treatment group with a mean difference of 0.41 kg (p=0.1864), and symptomatic hypoglycemia occurred in 3.4% of patients in the treatment group compared to 1.2% of patients in the placebo group.[10] Patients were then followed for 52 weeks thereafter in order to evaluate long term A1c efficacy of lixisenatide. After 76 weeks of treatment, lixisenatide was shown to significantly reduce the A1c by 1.1% vs. 0.6% in placebo.[10] This trial showed that the addition of lixisenatide to pioglitazone ± metformin can improve glycemic control without significantly increasing the patient's risk for symptomatic hypoglycemia.

GetGoal—L

Unlike the previous trials which looked at the addition of lixisenatide to only oral medications, GetGoal-L was a randomized, double blind, placebo controlled, parallel, multicenter, multinational study involving 496 patients inadequately controlled on both basal insulin ± metformin (79%). Baseline characteristics included patients with type 2 diabetes for an average of 12.5 years, mean A1c of 8.4%, metformin dose of ~2000 mg daily, average basal insulin use of 3.1 years, and a mean basal insulin dose of 55 units. Of the patients in the study, 248 (50%) were on insulin glargine, 198 (40%) were on NPH, 43 (9%) were on insulin detemir, and 8 (2%) were on premix insulin. Patients were randomized to receive either lixisenatide 20 mcg daily or placebo added to their current medication regimen for 24 weeks. The addition of lixisenatide provided improved glycemic control with a mean A1c change from baseline of about -0.6% compared to -0.3% with placebo (p=0.0002). A higher percentage of patients were able to attain a goal A1c <7% in the lixisenatide group compared to placebo (28.3% vs. 12%, p<0.0001). Of the patients in the lixisenatide group, 14.5% were able to successfully reach an A1c goal of <6.5% while only 3.8% were able to obtain that goal on placebo (p=0.0003). There was also a significant improvement in the PPG levels for patients on lixisenatide with a mean difference of 68.4 mg/dl (p<0.0001). Patients on lixisenatide lost a net average of 1.5 kg compared to placebo (p<0.0001) and had a greater reduction in basal insulin requirement (mean difference of 3.7 units/day, p=0.012) by 24 weeks. Symptomatic hypoglycemia and rate of discontinuation due to adverse events were comparable between the two groups (26.5% vs. 21.0% and 7.6% vs. 4.8%, respectively).[11] This trial demonstrated that lixisenatide can be an option for patients with uncontrolled diabetes who are not a candidate for meal time insulin.

GetGoal—X

Among all of the GetGoal clinical trials, GetGoal-X was the only trial that compared lixisenatide to an active control. GetGoal-X is a randomized, open label, comparator controlled, phase III trial involving 639 patients with type 2 diabetes inadequately controlled on metformin. Baseline A1c for the lixisenatide group was 8.03%, whereas the exenatide group was 8.02%. Both groups had an average metformin dose of approximately 2000 mg daily. Patients were randomized to lixisenatide 20 mcg once daily or exenatide 10 mcg twice daily. The purpose of the study was to investigate whether lixisenatide was non-inferior to exenatide in efficacy and safety in patients with type 2 diabetes inadequately controlled with metformin. In the trial, 318 patients were treated with lixisenatide and 316 were treated with exenatide for a total treatment period of 24 weeks. At the conclusion of the trial, lixisenatide was shown to be non-inferior to exenatide in reducing A1c. The mean reduction from baseline A1c in the lixisenatide group was -0.79% ± 0.05 and -0.96% ± 0.05 for the exenatide group. The lixisenatide treatment group was able to achieve a goal A1c < 7% in 48.5% of their patients while the exenatide group was able to obtain 49.8%. There were similar success rates for patients reaching a goal A1c <6.5% with lixisenatide having a success rate of 28.5% vs. 35.4% in exenatide. Reduction in body weight for the lixisenatide group was 2.96 kg compared to 3.98 kg with exenatide. The incidence of nausea was lower in the lixisenatide group at 24.5% of the patients compared to 35.1% in the

Table 2 | Most Common Adverse Effects for Lixisenatide.[5,7-12]

Adverse events	Lixisenatide	Placebo	Exenatide
Nausea	20.2 to 26.2%	4.1 to 10.6%	35.1%
Vomiting	6.7 to 13.3%	0 to 3.7%	13.3%
Symptomatic hypoglycemia[a]	2 to 26.5%	0.6 to 12.3%	7.9%
Severe hypoglycemia[b]	0 to 1.2%	0%	0%
Discontinuation due to adverse events	2.5 to 10.4%	0.8 to 5.0%	13.0%

[a]Defined as a glucose level of < 60 mg/dL with a prompt recovery after the administration of glucose, carbohydrates, or a glucagon injection.
[b]Defined as either a glucose level < 36 mg/dL or patient required assistance from another person in order to correct sugar levels.

exenatide group ($p<0.05$). Along with a lower average of patients experiencing a side effect, the incidence of symptomatic hypoglycemia was lower in the lixisenatide group compared to the exenatide group (2.5% vs. 7.9%, $p<0.05$).[12] In GetGoal-X, lixisenatide combined with metformin demonstrated non-inferiority to exenatide with metformin in terms of reduction in A1c, weight loss, and incidence of hypoglycemia.

Discussion

The results of these studies provided evidence that lixisenatide can be used with other common diabetic agents in order to provide additional glycemic control in patients with type 2 diabetes. In the studies mentioned, lixisenatide was used in combination with metformin, sulfonylureas, basal insulin, and/or thiazolidinediones. The addition of lixisenatide improved A1c and weight from baseline in each of the respective studies compared to placebo while having a minimal GI side effects. When lixisenatide was compared to exenatide for glycemic control, lixisenatide was deemed non-inferior, with both medications showing an improvement in A1c and weight from baseline.

Adverse Reactions

When lixisenatide is administered as monotherapy, with metformin, or pioglitazone ± metformin, hypoglycemia episodes are 2%, 3%, and 3%, respectively.[6] However, the risk for hypoglycemia increases when lixisenatide is administered with other diabetic agents such as basal insulin and/or a sulfonylurea. Lixisenatide administered with a sulfonylurea ± metformin, basal insulin ± metformin, or basal insulin -and a sulfonylurea, hypoglycemic episodes were estimated at 15%, 28%, and 47%, respectively. The most common adverse effects seen with the administration of lixisenatide was nausea and vomiting compared to placebo. Among the 11 main GetGoal clinical trials, nausea ranged from 16.3% to 50%, vomiting ranged from 2.8% to 13.3%, and discontinuation from medication due to any related side effects ranged from 2.5% to 10.4%.[6] The use of lixisenatide also resulted in side effects significant for headache, diarrhea, dizziness, and abdominal pain compared to placebo, however these were only reported in a handful of patients in the trials.[5,6] **Table 2** provides the most common side effects associated with the administration of lixisenatide compared to placebo in the aforementioned GetGoal trials. Pancreatitis was seen in 21 patients during the clinical trials, as well as post-marketing reports with lixisenatide. Acute kidney injury has also been observed in post-marketing reports, which is thought to be caused by the drug's ability to affect hydration status due to nausea and vomiting. Due to these post-marketing reports, patients should not be initiated on lixisenatide if they have a history of pancreatitis or develop signs and symptoms related to the disease. Caution should be used in patients who have renal dysfunction and the medication is contraindicated when eGFR drops below 15 ml/min.[6]

Precautions and Drug Interactions

Due to its mechanisms of action, lixisenatide delays gastric emptying which may reduce absorption of orally consumed medications or products. Like many other GLP-1 agonists, gastric emptying can be delayed. Medications such antibiotics, acetaminophen, and oral contraceptives may need to be dosed 1 hour prior or 11 hours after lixisenatide injections in order to be effective and maintain appropriate concentrations in the body. Lixisenatide has not been studied in patients with gastroparesis or pancreatitis, therefore it is not recommended in these populations.[6]

Table 3 | A1c Reductions of GLP-1 Agonists.[13-15]

Medication	A1c reduction (%)	Use w/ basal insulin
Lixisenatide	0.7 to 1.0	Yes
Exenatide	0.8 to 1.5	No
Exenatide LAR	1.3 to 1.9	Yes
Liraglutide	1.1 to 1.5	Yes
Albuglutide	0.3 to 0.9	Yes
Dulatglutide	0.7 to 1.6	No

LAR = long-acting release

Dosing and Administration

The recommended initial starting dose for lixisenatide is 10 mcg subcutaneously for 14 days followed by an increase in dose to 20 mcg once daily starting at day 15 of therapy. Maintenance dose is maintained at 20 mcg once daily. There is no dose adjustment for patients with renal impairment. Patients with reduced renal function (eGFR: 15-30 ml/min/1.73m^2) should use lixisenatide with caution. In patients with an eGFR < 15 ml/min/1.73m^2, the use of lixisenatide is contraindicated.[6] There have been no studies to date that have evaluated hepatic dysfunction with lixisenatide, however hepatic dysfunction is not likely to affect the pharmacokinetics of the medication.[6] The pen comes in two different pre-filled syringes: a 50 mcg/mL solution in a green prefilled pen (3 mL) and a 100 mcg/mL solution in a burgundy prefilled pen (3 mL). Each pen provides 14 doses. The pen is to be administered in the abdomen, thigh, or upper arm 1 hour prior to the largest meal of the day. As with other injectable products such as insulin, proper education and counseling is imperative in order to successfully use the medication.

Comparison Amongst GLP-1 Agonists

There has been a rapid growth in the development of GLP-1 agonists for the treatment of type 2 diabetes. Specific properties of the medications such as use with insulin, patient preferences, duration of action, and A1c reductions from baseline all determine which option is selected. Lixisenatide and exenatide injection are similar to native GLP-1 due to their short acting properties. By having a short half-life post injection, these medications have the ability to delay gastric emptying and reduce postprandial glucose excursions without causing desensitization. Long acting GLP -1 agonists such as dulaglutide, albiglutide, exenatide ER, and liraglutide can all lead to desensitization to the gastric emptying effect due to longer durations of action.[5] **Table 3** provides a summary of GLP-1 agonist efficacy in terms of A1c reduction from baseline as well as use with basal insulin.

Summary

Lixisenatide (Adlyxin®) is a once daily injection recently approved for the treatment of type 2 diabetes in combination of oral glucose lowering agents and/or basal insulin to help achieve glycemic control. Eleven phase III clinical trials have validated lixisenatide's efficacy and safety, while also establishing its place in therapy when used with other diabetic agents. This efficacy has also been directly compared to another established GLP-1 ago-

nist, exenatide (Byetta®) in the GetGoal-X trial. Results from this study showed that, when compared to exenatide, lixisenatide was non-inferior in improving glycemic control with reduced frequency of GI side effects. Across all the GetGoal clinical trials, reductions in baseline A1c ranged from 0.7% to 1.0%, while discontinuations due to adverse events ranged from 2.5% to 10.4%. The trials also showed a significant improvement in PPG compared to placebo. Compared to other GLP-1 agonist, lixisenatide has similar reductions in A1c and can be used with basal insulin to improve glycemic control. The once daily dosing and one-step increase to maintenance dose allow for lixisenatide to be an additional treatment options for patients with type 2 diabetes.

References

1. Centers for Disease Control and Prevention (CDC) 2014. More than 29 Million Americans have Diabetes; 1in 4 doesn't know. http://www.cdc.gov/media/releases/2014/p0610-diabetes-report.html. Accessed December 1, 2016.
2. American Diabetes Association. Standards in Medical Care in Diabetes. Diabetes Care. 2016;39(Suppl. 1): S52–S54 | DOI: 10.2337/dc16-S001
3. Handelsman Y, Mechanick JI, Blonde L, et al. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for Developing a Diabetes Mellitus Comprehensive Care Plan. Endocrine Practice 2011;17:(Suppl 2): 1-52. EL 4, NE CPG.
4. Holst JJ, Knop FK, Vilsbol T, et al. Loss of INcretin Effect is a Specific Important, and Early Characterisitc of Type 2 Diabetes. Diabetes Care. 2011;(Supplement 2) S251-S257; DOI: 10.2337/dc11-s227
5. Bain, SC. The clinical development program of lixisenatide: a once-daily glucagon-like peptide-1 receptor agonist. Diabetes Ther. 2014;5(2):367–383.
6. Adlyxin [package insert]. Ridgefield, NJ: Sanofi; 2016.
7. Fonseca VA, Alvarado-Ruiz R, Raccah D, et al. Efficacy and Safety of the Once-Daily GLP-1 Receptor Agonist Lixisenatide in Monotherapy: A randomized, double-blind, placebo-controlled trial in patients with type 2 diabetes (GetGoal-Mono). Diabetes Care. 2012;35(6): 1225-1231.
8. Ahrén B, Dimas AL, Miossec P, et al. Efficacy and safety of lixisenatide once-daily morning or evening injections in type 2 diabetes inadequately controlled on metformin (GetGoal-M). Diabetes Care. 2013;36(9): 2543-2550.
9. Rosenstock J, Hanefeld M, Shamanna P, et al. Beneficial effects of once-daily lixisenatide on overall and postprandial glycemic levels without significant excess of hypoglycemia in type 2 diabetes inadequately controlled on a sulfonylurea with or without metformin (GetGoal-S). Journal of Diabetes & its Complications. 2014;28(3): 386-392.
10. Pinget M, Goldenberg R, Niemoeller E, et al. Efficacy and safety of lixisenatide once daily versus placebo in type 2 diabetes insufficiently controlled on pioglitazone (GetGoal-P). Diabetes, Obesity and Metabolism. 2013;15(11): 1000-1007.
11. Riddle MC, Aronson R, Home P, et al. Adding once-daily lixisenatide for type 2 diabetes inadequately controlled by established basal insulin (GetGoal-L). Diabetes Care. 2013;36 (9): 2489-2496.
12. Rosenstock J, Raccah D, Koranyi L, et al. Efficacy and safety of lixisenatide once-daily vs exenatide twice-daily in type 2 DM inadequately controlled on metformin (GetGoal-X). Diabetes. 2011;60(Suppl 1): A33.
13. Tanzeum [package insert]. Philadelphia, PA: GlaxoSmithKline; 2014.
14. Ely Lilly 2016. Proven glycemic control with fewer injections. https://www.trulicity.com/healthcare-professionals-clinical-study.html. Accessed December 06, 2016.
15. Archer M, Steinvoort C, & Oderda G. Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists Drug Class Review. http://www.health.utah.gov/pharmacy/ptcommittee/files/Criteria%20Review%20Documents/05.13/05.13%20GLP-1%20Receptor%20Agonist%20Drug%20Class%20Review.pdf. Accessed December 6, 2016.

PharmaNote®

Published by the UF Family Practice Residency Program and the Departments of Community Health & Family Medicine and Pharmacotherapy & Translational Research

University *of* Florida

Editor-in-Chief
John G. Gums, PharmD, FCCP

Managing Editor
Jason Powell, PharmD

Associate Editor
R. Whit Curry, MD

Assistant Editor
Andrew Y. Hwang, PharmD, BCPS