PharmaNote®
Vol. 37, Issue 10 July 2022 Established 1985

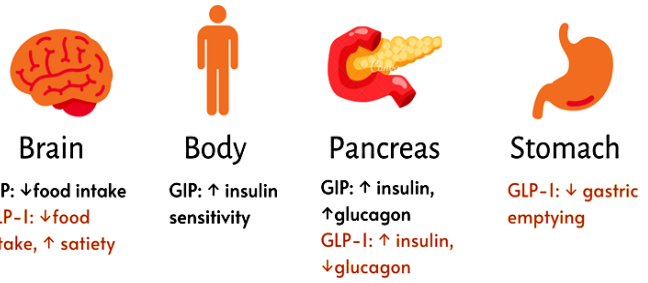
Mounjaro® (Tirzepatide): A Sweeter Outlook for Patients with Type 2 Diabetes

Shannon Komisarchik, PharmD

Diabetes is a chronic disease that affects people worldwide, including nearly 37.3 million Americans or about 11.3% of the US population as of January 2022.[1] Of this population nearly 95% have Type 2 Diabetes (T2DM). Risk factors for developing T2DM include poor diet, lack of exercise, tobacco use, and elevated body mass index (BMI).[2] Without proper diabetic management, medical complications can ensue and cause blindness, kidney failure, heart attack, stroke and even limb amputation.[2] Thus, a multidimensional approach including proper lifestyle, diet, and medication management is crucial to combatting the consequences of diabetes. The current American Diabetes Association (ADA) treatment guidelines endorse use of metformin as a first-line therapy in addition to comprehensive lifestyle modification.[3] Yet, additional medications are often needed to achieve glycemic control. Other classes of approved antihyperglycemic drugs include sodium glucose co-transporter-2 inhibitors (SGLT-2i), sulfonylureas, thiazolidinediones, glucagon-like peptide-1 (GLP) receptor agonists, as well as short and long-acting insulins. Medication therapy is selected in accordance with guideline recommendations and further tailored on patient characteristics such as renal function, cardiovascular risk, medication cost, potential side effects, and efficacy.

Incretin hormones such as glucagon-like peptide (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) play a large role in postprandial insulin release and ultimately both increase glucose clearance, consequently lowering serum blood glucose levels as part of normal pathophysiology. Patients with diabetes often exhibit a decreased incretin effect due to lower levels of circulating GLP-1 mediated by either less secretion by the gut or increased clearance. Studies continue to investigate the underlying pathophysiology behind the diminished incretin effect.[4] Currently marketed GLP-1 receptor agonists include exenatide (given twice daily), liraglutide, and lixisenatide (given daily), and once weekly agents such as exenatide extended-release, albiglutide, and dulaglutide.[5] These agents reduce serum glucose levels by activating GLP-1 receptors in the pancreas, resulting in stimulated insulin release while reducing glucagon release. These mechanisms are glucose dependent resulting in a lower risk for hypoglycemia in patients using these agents for treatment.[6] Additionally, select GLP-1 receptor agonists such as dulaglutide, have been shown to provide a reduction in cardiovascular events in adults with and without cardiovascular disease.[7] As depicted in **Figure 1**, GIP plays a significant role in lipid metabolism, fat deposition as well as working in areas of the brain that are known to control appetite.[8] GIP has also shown direct effects on insulin sensitivity in those with T2DM.[9]

Figure 1 | Comparison of GLP-1 and GIP Actions[10]



Mounjaro™(tirzepatide) is a novel dual GLP-1 (glucagon-like peptide-1) and GIP (glucose-dependent insulinotropic polypeptide) receptor agonist, combining the actions of both incretins into one medication. This therapy is the first of its kind approved by the FDA. Tirzepatide was FDA approved in May 2022 for use in adults with type 2 diabetes mellitus, to be used in combination with diet and exercise to achieve improved glycemic control. This article aims to explore the clinical uses, pharmacological profile, and distinctive properties of tirzepatide.[11]

Pharmacology

Tirzepatide was proven to enhance both first and second phase insulin secretion, while also reducing glucagon levels. Data showed that the pharmacokinetics between those without and with T2DM were similar. Steady state was achieved after 4 weeks of weekly administration, proportional increases with exposure. As seen in **Table 1**, the average steady state was 10.3 liters in T2DM patients with subcutaneous delivery. Patient characteristics such as age, gender, race/ethnicity, and weight did not show clinical relevance to the pharmacokinetic profile of the drug.[11]

IN THIS ISSUE

In vitro studies showed a low incidence for tirzepatide to inhibit or induce CYP enzymes. Tirzepatide functions to delay gastric emptying and therefore influences the absorption of coadministered oral medicines. This effect was demonstrated in studies, and showed that the extent of delayed gastric emptying was similar to selective long acting GLP-1 receptor agonists.[18] The delayed gastric emptying was highest when a single 5 mg dose was given, however decreased after additional doses. As a result of delayed gastric emptying, caution should be used when taking concomitant oral medications, especially those with narrow therapeutic index such as warfarin. Additionally, patients taking oral hormonal contraceptives should be advised to switch to a non-oral option, or add a barrier method for 4 weeks after starting tirzepatide and for 4 weeks with each dose increase.[11]

Clinical Trials

Five clinical trials, consisting of the SURPASS trial series, were conducted to establish tirzepatide efficacy as an add-on therapy to diet and exercise to improve glycemic control in those with T2DM. In SURPASS-1, tirzepatide was studied as monotherapy while in SURPASS-2,-3, and -4 it was studied as an add-on therapy to metformin, sulfonylureas, and/or SGLT2i. SURPASS-5 studied tirzepatide in combination with basal insulin with or without metformin. In the respective trials, tirzepatide (5 mg, 10mg, 15 mg) was compared with placebo, semaglutide 1 mg, insulin degludec, and/or insulin glargine. The following section will review these trials with a summary of the reduction in HbA1C and changes in body weight shown in **Table 2**.

SURPASS-1[12]

The SURPASS-1 study was conducted as a 40-week, double blind, randomized, placebo-controlled, phase 3 study that took place over 52 medical research facilities and hospitals located in the United States, Japan, Mexico, and India. Inclusion criteria consisted of adults of at least 18 years of age who were type-2 diabetic and uncontrolled with diet and exercise efforts. Eligible subjects were required to have a HbA1C of 7.0% to 9.5% and a body mass index (BMI) of 23 kg/m2 or more. The participants were naive to injectable diabetic treatments such as insulin and GLP-1 receptor agonists. Participants were randomly assigned (1:1:1) to receive a once-weekly subcutaneous injection of either tirzepatide 5 mg (n=121), 10 mg (n=121), 15mg (n=120) or placebo (n=115). The doses of tirzepatide were titrated in a fixed 2.5mg dose increment every 4 weeks until randomized target dose was achieved at week 4,12, and 20 in the respective tirzepatide groups.[12] Key exclusion criteria included patients with Type 1 diabetes and history of pancreatitis.[12]

Clinically significant results were indicated at a primary endpoint of mean change from baseline HbA1C at 40 weeks of treatment with tirzepatide. The key secondary endpoints included mean change from baseline body-weight, mean change from baseline in fasting serum glucose, and percent of subjects with HbA1C target less than 7.0% and less than 5.7%.[12]

SURPASS-2[13]

The SURPASS-2 clinical trial set out to discover the efficacy, safety, and tolerability of tirzepatide assessed in comparison to semaglutide 1 mg. The design of the study was an international, randomized, open-label phase 3 noninferiority trial that compared semaglutide to tirzepatide. The participants (n=1878) were randomly assigned in a 1:1:1 fashion to receive a subcutaneous injection of tirzepatide 5mg (n=470), 10mg (n=469), or 15mg (n=470) or semaglutide 1mg (n=469). Tirzepatide was started at 2.5mg once weekly and then increased by 2.5mg every 4 weeks until the randomized target dose was achieved and then maintained for the duration of the trial. Semaglutide was started at 0.25mg once weekly and then doubled every 4 weeks until mg dose was achieved and maintained for the duration of the trial. Key inclusion criteria for this trial required adults 18 years of age or older, T2DM diagnosis that was uncontrolled with metformin, HbA1C of 7.0-10.5% and body-mass-index of greater than 25.[13] Exclusion criteria consisted of patients with type 1 diabetes and history of pancreatitis.

Tirzepatide was found to be non-inferior and superior to semaglutide with regards to the primary endpoint which was the average change in HbA1C level from baseline to 40-weeks of follow-up. The key secondary endpoints were the change in body-weight from baseline to week 40 and the fulfillment of participants with HbA1C levels of 7.0% and 5.7%.[13]

Table 1 | Select Tirzepatide Pharmacokinetics[11]

Absorption	
T_{max}[a]	8-72 hours
Bioavailability	80%
Distribution	
V_{ss}[b]	10.3 L
Protein Binding	99%
Metabolism	
$T_{1/2}$[c]	~5 days
	Proteolytic cleavage
Elimination	
	Urine
	Feces

[a]Time to maximum concentration; [b]Steady state volume of distribution; [c]Half-life

SURPASS-3[14]

The SURPASS-3 clinical trial assessed the efficacy, safety and tolerability of tirzepatide at 5, 10 and 15 mg in comparison to titrated insulin degludec. Patients were also being treated concomitantly with metformin and/or an SGLT2i for 3 months minimum. The study design was an open-label, parallel group, multicenter (122 sites), multinational (13 countries), phase 3 study. The participants were randomized (1:1:1:1) to once-weekly subcutaneous injection of tirzepatide 5, 10, 15mg or once-daily subcutaneous injection of titrated insulin degludec, and categorized according to country, HbA1C and concomitant use of oral antihyperglycemic medications. The starting dose of tirzepatide was 2.5mg and titrated up by 2.5 mg to the assigned dose every 4 weeks. Insulin degludec was started at 10 units daily and titrated once weekly to a fasting self-monitored blood glucose level of < 90mg/dL. Key inclusion criteria for this clinical trial required patients greater than 18 years of age with a baseline HbA1C of 7.0%-10.5% with a BMI of 25 kg/m2, and insulin naive status.[14] Key exclusion criteria were patients with type 1 diabetes and history of pancreatitis.[13]

Tirzepatide at 5, 10, and 15 mg was shown to be superior to titrated insulin degludec. The primary endpoint was the mean change from baseline in HbA1C at week 52 to determine non-inferiority of tirzepatide 10 mg or 15 mg, or both compared to insulin degludec. Key secondary endpoints were non-inferiority of tirzepatide 5mg compared to insulin degludec in mean change

from baseline HbA1C at 52 weeks, superiority of all tirzepatide doses compared to insulin degludec in average change from baseline HbA1C and body weight, as well as percent of participants with HbA1C of <7.0% at study completion.[14]

SURPASS-4[15]

The SURPASS-4 clinical trial was conducted over a period of 52 to 104 weeks with the purpose of assessing the cardiovascular (CV) safety, efficacy and safety of tirzepatide in comparison to insulin glargine. The study design was an open-label, parallel group, phase 3 study conducted over 187 sites within 14 countries in 5 continents. The participants were randomized (1:1:1:3) to receive either a subcutaneous injection of tirzepatide 5mg (n=329) 10mg (n=328),15mg (n=338) or glargine 100 U/mL (n=1000) titrated to attain fasting blood glucose of <100mg/dL. Tirzepatide doses were started at 2.5mg weekly and titrated by 2.5mg every 4 weeks until target dose was reached and maintained. The inclusion criteria consisted of adults aged 18 years and older with T2DM, treated with any combination of metformin, sulfonylurea, or BMI of 25kg/m2 or higher, and an established CV disease or high risk of CV events. Key exclusion criteria were patients with Type 1 diabetes and history of pancreatitis.[15] The primary endpoint of change in HbA1C from baseline to 52 weeks showed greater reduction in tirzepatide as compared with glargine. Secondary endpoints included change in body weight from baseline to 52 weeks and reaching a HbA1C of <7.0%. The study found that tirzepatide did not possess excess CV risk according to the collection of major adverse cardiovascular events (MACE) such as CV death, myocardial infarction stroke, and hospitalization from unstable angina.[15]

SURPASS-5[16]

The SURPASS-5 study was conducted as a 40-week phase 3 randomized trial taking place at 45 sites in 8 countries in those with uncontrolled T2DM. It assessed the efficacy of tirzepatide in participants taking insulin glargine with or without metformin versus placebo. The study participants were randomized in a 1:1:1:1 ratio to get a subcutaneous injection of 5mg (n=116), 10mg (n=119) or 15mg (n=120) tirzepatide or a volume-matched placebo injection (n=120). The tirzepatide was started at 2.5mg weekly and titrated up by 2.5mg every 4 weeks until the target dose was reached. The inclusion criteria consisted of adults with a baseline HbA1C of 7.0-10.5% and BMI of at least 23kg/m^2. Key exclusion criteria were patients with Type 1 diabetes and history of pancreatitis.[16]

The results of this study showed statistically significant improvements in glycemic control after 40 weeks in those treated with tirzepatide + insulin glargine versus placebo + titrated insulin glargine. The primary endpoint was average change from baseline in HbA1C at week 40, while secondary endpoints included mean change in body weight and percent of patients achieving HbA1C <7.0%. 16

Table 2 | Summary of Primary Outcomes[12-16]

Trial	Treatment Arms	Mean HbA1c[2] Reduction from Baseline (%)	Mean HbA1c Difference	Mean Weight Loss from Baseline (kg)	Mean Weight Loss Difference
SURPASS-1[12]	TZP[1] 5mg	-1.87	-1.91 (p<0.0001)	-7.0	-6.3 (p<0.0001)
	TZP 10mg	-1.89	-1.93 (p<0.0001)	-7.8	-7.1 (p<0.0001)
	TZP 15mg	-2.07	-2.11 (p<0.0001)	-9.5	-8.8 (p<0.0001)
	Placebo	0.04	—	-0.7	—
SURPASS-2[13]	TZP 5mg + metformin	-2.01	-0.15	-7.6	-1.9 (p<0.001)
	TZP 10mg + metformin	-2.24	-0.39 (p<0.001)	-9.3	-3.6 (p<0.001)
	TZP 15mg + metformin	-2.3	-0.45 (p<0.001)	-11.2	-5.5 (p<0.001)
	Semaglutide 1 mg	-1.86	—	-5.7	—
SURPASS-3[14]	TZP 5mg + metformin +/- SGLT2i[3]	-1.93	-0.59 (p<0.001)	-7.5	-9.8 (p<0.001)
	TZP 10mg + metformin +/- SGLT2i	-2.2	-0.86 (p<0.001)	-10.7	-13.0 (p<0.001)
	TZP 15mg + metformin +/- SGLT2i	-2.37	-1.04 (p<0.001)	-12.9	-15.2 (p<0.001)
	Insulin degludec	-1.34	—	-2.3	—
SURPASS-4[15]	TZP 5mg + metformin +/- SGLT2i or SU[4]	-2.24	-0.8 (p<0.0001)	-7.1	-9.0 (p<0.001)
	TZP 10mg + metformin +/- SGLT2i or SU	-2.43	-0.99 (p<0.0001)	-9.5	-11.4 (p<0.0001)
	TZP 15mg + metformin +/- SGLT2i or SU	-2.58	-1.14 (p<0.0001)	-11.9	-13.5 (p<0.0001)
	Insulin glargine	-1.44	—	-1.9	—
SURPASS-5[16]	TZP 5mg +/- metformin	-2.11	-1.24 (p<0.001)	-5.4	-7.1 (p<0.001)
	TZP 10mg +/- metformin	-2.40	-1.53 (p<0.001)	-7.5	-9.1 (p<0.001)
	TZP 15mg +/- metformin	-2.34	-1.47 (p<0.001)	-8.8	-10.5 (p<0.001)
	Placebo	-0.86	—	-1.6	—

[1]Tirzepatide; [2]Hemoglobin A1c; [3]Sodium-glucose co-transporter 2 inhibitor; [4]Sulfonylureas

Table 3 | Common Adverse Effects with Tirzepatide[12-16]

Adverse Effect	Incidence Rate
Nausea	12 –24%
Vomiting	2—12.5%
Diarrhea	12—22%

Ongoing Clinical Trials

There are currently several ongoing clinical trials for assessing tirzepatide use. SURPASS-6 is assessing tirzepatide as a potential alternative to initiating prandial insulin in those already taking basal insulin to treat T2DM with a primary endpoint of change in HbA1C after 52 weeks of treatment. Another trial, SURPASS-CVOT is investigating tirzepatide in the setting of patients with T2DM with underlying atherosclerotic cardiovascular disease and overweight status versus dulaglutide, which has a confirmed cardioprotection. Furthermore, the SURMOUNT trials are investigating tirzepatide as a weight loss agent in those with obesity, with and without T2DM.[17]

Adverse Effects

The most common side effects of tirzepatide were related to gastrointestinal distress and included nausea, diarrhea, and vomiting with the rate at which these side effects were experienced being dose dependent, as shown in Table 3.[12-16] Other common adverse drug effects observed in tirzepatide was a decreased appetite, ranging from 3.8% to 18.9% and 3% to 7% of tirzepatide patients reported injection site reactions, whereas only 1% reported this in the placebo cohort.[16] Regarding hypoglycemia risk, the incidence was low in both phase 2 and 3 trials. In SURPASS-3 hypoglycemia was observed in 0.6% in the 5mg TZP group, 0.2% in the 10mg TZP group, and 1.7% in the 15mg TZP group. As far as those receiving semaglutide, there was a 0.4% report of hypoglycemia.[17]

Contraindications

Tirzepatide is contraindicated in patients with current and past personal or family history of Medullary Thyroid Carcinoma, with the FDA even listing this as a black box warning. Risk of thyroid C cell cancer was observed in both male and female rats at clinically relevant exposures. Patients should be counseled on the risk of MTC and symptoms of thyroid tumors.[11] Additional warnings associated with tirzepatide can be seen in Table 4.

Special Populations

There was no impact on PK with a dose of 5mg on those with mild, moderate, severe and ESRD as compared to those with normally functioning kidneys. Other doses have not been fully studied to date. For hepatic impairment, there was no relevant impact on pharmacokinetics with a 5mg dose in patients with mild, moderate, severe hepatic function as compared to those with normally functioning liver. Other doses have not been fully studied to date.[11]

In women who are pregnant or lactating, there is no current data on the presence of tirzepatide in breast milk or effects it may have on a breastfed infant. For tirzepatide use in pregnant women, current data is insufficient to evaluate risk for drug related birth-defects, miscarriage risk, and other maternal-fetal adverse effects. However, animal studies showed fetal risk from exposure to tirzepatide such as fetal growth reduction. Tirzepatide should only be used if the benefits outweigh the risks of the mother and fetus.[11]

Dosage and Administration

Tirzepatide is dosed as a once-weekly subcutaneous injection that can be administered at any time of day without regard to meals. Location of injection should be confined to the abdomen, thigh or upper arm. Sites should be rotated, and the medication should be inspected before injection, ensuring it is clear, colorless/slightly yellow. Tirzepatide is supplied as a pre-filled, pre-attached needle, single-dose pen that is stored in the refrigerator.[11] If necessary, each pen can be stored at room temperature for up to 21 days. Tirzepatide should never be placed in a freezer.[11]

Tirzepatide pen injections are available in multiple strengths such as 2.5 mg/0.5 mL, 5 mg/0.5 mL, 7.5 mg/0.5 mL, 10 mg/0.5 mL, 12.5 mg/0.5 mL, and 15 mg/0.5 mL.[11] The starting dose is a 2.5 mg subcutaneous injection once a week for initiation of treatment only, and is not for glycemic control. After 4 consecutive weeks of this, the dose should be increased to 5mg subcutaneous weekly injection. If further glycemic control is necessary, then increase by 2.5mg after a minimum of 4 weeks on the current dose. The maximum dose is 15mg subcutaneous injection weekly. If there is a missed dose, the patient should administer as soon as possible within 4 days after the missed dose. If >4 days have gone by, skip the missed dose and administer the next dose as regularly scheduled. The day of week can be changed as long as at least 3 days have passed between doses.[11]

Cost and Availability

Pricing is predicted to be around $5,500 to $7,500 annually and is thought to be a cost effective option according to the Institute for Clinical and Economic Review (ICER). In contrast, current injectable GLP-1 receptor agonists are priced around $2,100-

Table 4 | Warnings and Adverse Reactions with Tirzepatide[11]

Adverse Reaction	Clinical Recommendation
Pancreatitis	Recommended discontinue use in patients with elevated triglycerides. Contraindicated in patients with history of pancreatitis.
Hypoglycemia	Noted with use of concurrent insulin or insulin secretagogues such as sulfonylureas. Recommend reducing dose of concomitant medications and counseling on symptoms of hypoglycemia.
Hypersensitivity	Discontinue use if hypersensitivity reactions such as eczema or urticaria occur. Use with caution in patient with history of angioedema and anaphylaxis.
Acute Kidney Injury	Manifested indirectly due to GI adverse effects (vomiting, diarrhea) leading to dehydration and eventual kidney injury if untreated. Caution use in malnourished patients.
Severe GI Disease	Not recommended in those with severe GI disease such as gastroparesis.
Acute Gallbladder Disease	Incidence of gallbladder disease (cholelithiasis, biliary colic, and cholecystectomy) seen in post-marketing reports. Caution use in patients with underlying conditions.

$2,500 per year. Tirzepatide is currently available to be ordered by pharmacies, however insurance coverage will vary. Manufacturer coupons of $25 for 30 day supply are available to assist commercially insured patients.[19]

Conclusion

Tirzepatide is a novel once-weekly medication for treating T2DM that demonstrates significant reductions in boh HbA1C and weight compared to multiple comparators. While the current FDA approval does not include weight loss, this effect was seen profoundly throughout the various SURPASS trials. Limitations of use include inability to be used in Type 1 diabetes and lack of studies for use in those with a history of pancreatitis. In conclusion, the data collected from the SURPASS trials show that tirzepatide delivers safe, positive results for glycemic control and weight loss that could change the standards of best care for patients with T2DM. Future studies will uncover other potential uses and benefits.

References

1. Centers for Disease Control and Prevention. National Diabetes Statistics Report website. https://www.cdc.gov/diabetes/data/statistics-report/index.html Accessed 05/23/22.
2. "Diabetes." World Health Organization, WHO, 10 Nov. 2021, https://www.who.int/news-room/fact-sheets/detail/diabetes
3. American Diabetes Association Professional Practice Committee; 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes—2022. Diabetes Care 1 January 2022; 45 (Supplement_1): S125–S143.
4. Jens Juul Holst, Mette Marie Rosenkilde, GIP as a Therapeutic Target in Diabetes and Obesity: Insight From Incretin Co-agonists, The Journal of Clinical Endocrinology & Metabolism, Volume 105, Issue 8, August 2020, Pages e2710–e2716, https://doi.org/10.1210/clinem/dgaa327
5. Hinnen D. Glucagon-Like Peptide 1 Receptor Agonists for Type 2 Diabetes. Diabetes Spectr. 2017;30(3):202-210. doi:10.2337/ds16-0026
6. Collins L, Costello RA. Glucagon-like Peptide-1 Receptor Agonists. [Updated 2022 Mar 31]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan.
7. Gerstein HC, Colhoun HM, Dagenais GR, et al. Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial. Lancet. 2019;394(10193):121-130. doi:10.1016/S0140-6736(19)31149-3
8. Adriaenssens AE, Biggs EK, Darwish T, et al. Glucose-dependent insulinotropic polypeptide receptor-expressing cells in the hypothalamus regulate food intake. Cell Metab. 2019;30(5):987-996.e6.
9. Mohammad S, Ramos LS, Buck J, et al. Gastric inhibitory peptide controls adipose insulin sensitivity via activation of cAMP-response element-binding protein and p110β isoform of phosphatidylinositol 3-kinase. J Biol Chem. 2011;286(50):43062-43070.
10. Samms RJ, Coghlan MP, Sloop KW. How may GIP enhance the therapeutic efficacy of GLP-1? Trends Endocrinol Metab. 2020;31(6):410-421.
11. MOUNJARO™ (tirzepatide) Injection, for subcutaneous use Initial U.S. Approval: 2022. Eli Lilly.
12. Rosenstock J, Wysham C, Frías JP, et al. Efficacy and safety of a novel dual GIP and GLP-1 receptor agonist tirzepatide in patients with type 2 diabetes (SURPASS-1): a double-blind, randomised, phase 3 trial [published correction appears in Lancet. 2021 Jul 17;398(10296):212]. Lancet. 2021;398(10295):143-155. doi:10.1016/S0140-6736(21)01324-6
13. Frías JP, Davies MJ, Rosenstock J, et al. Tirzepatide versus Semaglutide Once Weekly in Patients with Type 2 Diabetes. N Engl J Med. 2021;385(6):503-515. doi:10.1056/NEJMoa2107519
14. Bernhard Ludvik, Francesco Giorgino, Esteban Jodar, Juan Pablo Frias, Laura Fernandez Lando, Katelyn Brown, Ross Bray, Ángel Rodriguez; 78-LB: Efficacy and Safety of Tirzepatide, a Dual GIP/GLP-1 Receptor Agonist, Compared with Insulin Degludec in Patients with Type 2 Diabetes (SURPASS-3). Diabetes 1 June 2021; 70 (Supplement_1): 78–LB. https://doi.org/10.2337/db21-78-LB
15. Del Prato S, Kahn SE, Pavo I, et al. Tirzepatide versus insulin glargine in type 2 diabetes and increased cardiovascular risk (SURPASS-4): a randomised, open-label, parallel-group, multicentre, phase 3 trial. Lancet. 2021;398(10313):1811-1824. doi:10.1016/S0140-6736(21)02188-7
16. Dahl D, Onishi Y, Norwood P, et al. Effect of Subcutaneous Tirzepatide vs Placebo Added to Titrated Insulin Glargine on Glycemic Control in Patients With Type 2 Diabetes: The SURPASS-5 Randomized Clinical Trial. JAMA. 2022;327(6):534–545. doi:10.1001/jama.2022.0078
17. Min, T., Bain, S.C. The Role of Tirzepatide, Dual GIP and GLP-1 Receptor Agonist, in the Management of Type 2 Diabetes: The SURPASS Clinical Trials. Diabetes Ther 12, 143–157 (2021). https://doi.org/10.1007/s13300-020-00981-0
18. Urva S, Coskun T, Loghin C, et al. The novel dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 (GLP-1) receptor agonist tirzepatide transiently delays gastric emptying similarly to selective long-acting GLP-1 receptor agonists. Diabetes Obes Metab. 2020;22(10):1886-1891. doi:10.1111/dom.14110
19. Institute For Clinical and Economic Review. ICER Publishes Evidence Report on Tirzepatide For Type 2 Diabetes. Jan 2022. https://icer.org/news-insights/press-releases/icer-publishes-evidence-report-on-tirzepatide-for-type-2-diabetes/

Drug Update:
New Indications and Dosage Forms
June 2022

Voquezna Triple Pak® (vonoprazan, amoxicillin, clarithromycin) Oral Tablet
New Molecular Formulation: Combination macrolide, penicillin, and potassium-competitive acid blocker use for the treatment of *H. pylori* used twice daily for 14 days

Vtama® (tapinarof) Topical Cream
New Molecular Entity: An-aryl hydrocarbon receptor agonist indicated for the treatment of plaque psoriasis in adults; specific mechanism of action unknown

Vivjoa® (oteseconazole) Oral Capsule
New Molecular Entity: Azole antifungal indicated to reduce the incidence of recurrent vulvovaginal candidiasis (RVVC) in females not of reproductive potential

PharmaNote®

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

University *of* Florida