Glucagon-like peptide-1 (GLP-1) receptor agonists

supplement to *Cafer's Psychopharmacology* 1/22/23

GLP-1 receptor agonists are type 2 diabetes medications, also called GLP analogs or incretin mimetics. The 3 most-prescribed GLP-1 receptor agonists are "-glutides"—mnemonic "glue tide". The other two GLP analogs are "-enatides"—mnemonic "in a Tide Pod". Two GLP analogs were recently approved for weight management. All GLP analogs were subcutaneous injectables until the arrival of Rybelsus (oral semaglutide) in 2020. The -glutides have been proven to reduce risk of cardiovascular events, while -enatides have not.

GLP analogs should not be used for type 1 diabetes.

Glucagon-like peptide-1 (GLP-1) receptor agonists, the "-tides"		
"Glue tide"... 	-glutides reduce cardiovascular risk. Liraglutide and semaglutide are approved for DM and weight loss.	Dulaglutide Liraglutide Semaglutide
..."in a Tide" Pod 	-enatides lower postprandial (rather than fasting) blood glucose —"after you eat a Tide Pod"	Exenatide Lixisenatide

Gastrointestinal side effects with GLP analogs are common, including nausea/vomiting and diarrhea, mainly during dose escalation. Rarely these drugs may be associated with acute pancreatitis or cholelithiasis, although causal link is questionable. GLP analogs do not damage the kidneys, but there have been cases of acute renal failure due to dehydration secondary to vomiting/diarrhea. Serious hypersensitivity reactions such as anaphylaxis and angioedema have occurred.

Thyroid tumors have been reported in rodents given GLP analogs and thyroid C-cell hyperplasia has been reported in humans. GLP analogs (other than lixisenatide) are contraindicated in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) or a family history of medullary thyroid carcinoma.

GLP analogs bind GLP-1 receptors in the brain involved in appetite regulation. These medications are considered neuroprotective. Neuropsychiatric reactions including suicidal thoughts have been reported with GLP analogs, although barely exceeding placebo and unlikely to warrant clinical concern (O'Neil et al, 2017). There is preclinical evidence that GLP analogs can attenuate behaviors that model abuse of substances including alcohol, cocaine, and nicotine.

Role of GLP analogs (and alternatives) in type 2 diabetes:

The goal of drug therapy is generally to keep hemoglobin A1C <7%.

The biguanide **metformin** (Glucophage) is the recommended first-line treatment of type 2 diabetes—"begin with the biguanide"—except in renal insufficiency with GFR <45. Metformin ($10, oral) works through several mechanisms including increased secretion of GLP-1. Metformin improves insulin resistance, causes modest weight loss, and reduces all-cause mortality. Even in nondiabetic individuals, metformin appears to slow the aging process, extending lifespan and healthspan.

When metformin is inadequate it should be augmented with (if affordable) either a GLP analog ($1,000, SC/oral) or a SGLT2-inhibiting "-gliflozin" drug ($500, oral). With -gliflozins "glucose flows in urine / SuGar LeakT into urine". SGLT2 inhibitors can cause genital yeast infections and gangrene. In order of popularity, the available SGLT2 inhibitors are **empagliflozin** (Jardiance), **canagliflozin** (Invokana), **dapagliflozin** (Farxiga), and **ertugliflozin** (Steglatro). SGLT2 inhibitors cause modest weight loss and decrease blood pressure via diuresis.

None of these first- and second-line options (metformin, -tides, -gliflozins) cause hypoglycemia when used as monotherapy.

If a -glutide or -gliflozin is unaffordable, a **sulfonylurea** ($10, oral) can be added to metformin—"a sulfonylurea can suffice". While GLP analogs increase insulin release in a glucose-dependent fashion, release of insulin with sulfonylureas is not dependent on blood glucose and thereby may lead to hypoglycemia, especially with **glyburide** (Micronase). The preferred sulfonylureas are **glimepiride** (Amaryl) and **glipizide** (Glucotrol)—"ride a 'zide if you can't buy a -tide, but bury glyburide". Another disadvantage of sulfonylureas is potential for weight gain. All diabetes medications with *generic* name starting with G cause weight Gain—glimepiride, glipizide, glyburide, and insulins glargine and glulisine.

Less effective that GLP analogs are the "gliptins" ($500, oral) which inhibit the breakdown of GLP-1 by dipeptidyl peptidase-4 (DPP-4)—keeping "GLP intact". The most-prescribed DPP-4 inhibitors are sitagliptin (Januvia) and linagliptin (Tradjenta). Gliptins are associated with acute pancreatitis. They reduce hemoglobin A1c by 0.5–1.0% but do not appear to decrease all-cause mortality. They are weight neutral—"weight just sits in line" with sitagliptin and linagliptin.

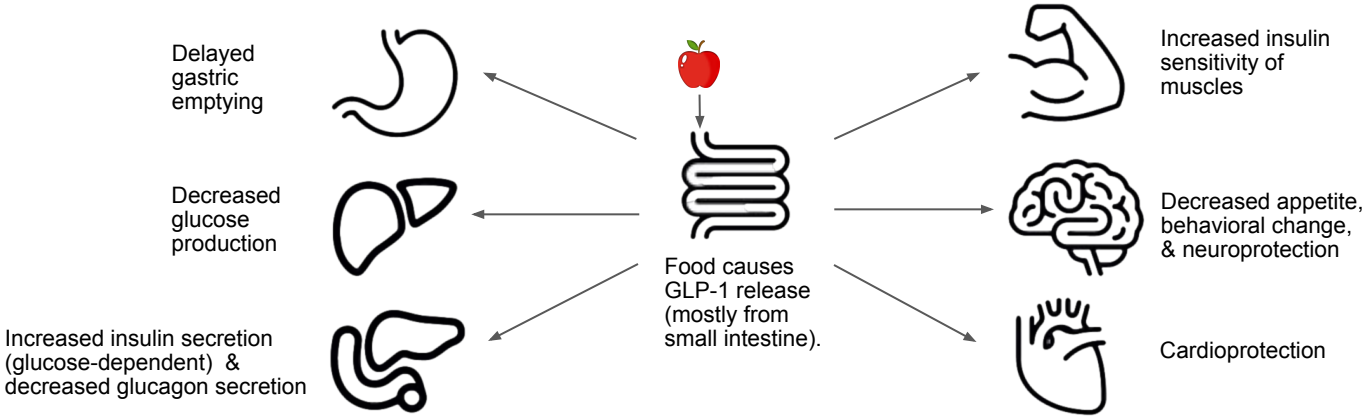
The **thiazolidinediones** (TZDs) should generally be avoided. TZDs including pioglitazone (Actos) and rosiglitazone (Avandia) increase risk of heart failure, anemia, and osteoporosis—"The glitter zone is The Zone of Danger". TZDs also have potential for large weight gain—"pig-glitazone" and "whole lotta Rosie".

Insulin is recommended if initial A1C is >9% or if glycemic control is inadequate with a combination of the above-mentioned drugs. Insulin is associated with weight gain. Two available products combine a GLP analog with insulin for once-daily SC injection. XULTOPHY [ZUL toh fye] pairs liraglutide with insulin degludec (Tresiba). SOLIQUA [soh LEE kwa] combines lixisenatide with insulin glargine (Lantus).

GLP-1 action on target tissues

Glucagon-like peptide-1 (GLP-1) is a hormone released from the gut after eating to decrease blood glucose by several mechanisms. GLP-1 is an incretin, i.e., hormone that increases insulin secretion. To restate, incretin increases insulin secretion. GLP-1 is not the only incretin, but it constitutes >90% of all endogenous incretin function. GLP analogs (-tides) are considered incretin mimetics

The structure of glucagon-**like** peptide-1 is "like" that of glucagon but GLP-1 and glucagon serve opposite functions. Glucagon, also known as hyperglycemic factor, is released by the pancreas to increase breakdown of glycogen in the liver thereby releasing glucose into the blood. Synthetic forms of glucagon are available for treatment of severe acute hypoglycemia, including the intramuscular Gvoke HypoPen and a nasal powder called Baqsimi [BAK see mee]—"come back to see me".



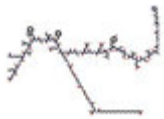
Glucagon-like peptide-1 (GLP-1) receptor agonists

aka the "-tides", GLP analogs, incretin mimetics

Rx 2021	GLP analog	Trade	Dosing	Indication	Reduce CV risk*	Effect	Details
#1	Liraglutide	VICTOZA	SC QD	DM2	Yes. Also reduces overall mortality–"Victory!"	↓ A1c 1.5%	Available with insulin degludec (Tresiba) in a prefilled pen as XULTOPHY [ZUL toh fye]
		SAXENDA	SC QD	**weight**		↓ 6% body weight	Placebo-corrected weight loss of 12 pounds. 63% of patients taking the drug lost ≥5% body weight. Less effective than Wegovy at FDA-approved dose
#2	Dulaglutide	TRULICITY	SC weekly	DM2	Yes	↓ A1c 1.5–1.8%	The most effective GLP agonist at reducing A1c. Relatively low incidence of injection site reactions
#3	Semaglutide	OZEMPIC	SC weekly	DM2	Yes	↓ A1c 1.5%	Lowers weight by about 9 pounds at the dose used for DM. Warning of increased risk of diabetic retinopathy
		RYBELSUS	**PO** QD	DM2	Unproven	↓ A1c 1%	Must be taken with no more than 4 ounces of plain water 30 minutes before the first meal of the day
		WEGOVY	SC weekly	**weight**	N/A	↓ 12% body weight	"We 'gon lose WEight with WEekly WEgovy". Higher semaglutide dose than Ozempic
#4	Exenatide	BYDUREON	SC weekly	DM2	Unproven	↓ A1c 1.5%	The only GLP analog that does not require titration because it has the lowest incidence of nausea (10%)
		BYETTA	SC **BID**			↓ A1c 1%	The only GLP analog requiring BID dosing. -Enatides (Byetta included) primarily decrease postprandial blood glucose, with limited impact on fasting glucose.
#5	Lixisenatide	ADLYXIN	SC QD	DM2	Unproven	↓ A1c 1%	The only GLP analog without a boxed warning of thyroid C-cell tumor risk. Available with insulin glargine (lantus) as SOLIQUA [soh LEE kwa].
New	Tirzepatide	MOUNJARO	SC weekly	DM2	Unproven	↓ A1c 2.3% ↓ 20% body weight	The first "twincretin" agonist of GLP-1 and glucose-dependent insulinotropic polypeptide (GIP), which is similar to GLP-1. Appears superior to others.

*The FDA has approved the use of -glutides to reduce the risk of major cardiovascular events (myocardial infarction, stroke, cardiovascular death) in adults with type 2 diabetes and established cardiovascular disease or multiple cardiovascular risk factors.

#149
2014
$735–$1000



Dulaglutide (TRULICITY)

DOO la GLOO tide / TRU li si tee

"Truly a Doula" glue tide

❖ GLP-1 receptor agonist

0.75
1.5
3
4.5 mg

FDA-approved for:
- ❖ Type 2 diabetes

Used off-label for:
- ❖ Weight loss

Don't let this mnemonic misguide you—GLP analogs should not be used during pregnancy.

Dulaglutide (Trulicity) is a GLP analog that reduces hemoglobin A1C by 1.5% to 1.8%, which is slightly more than other GLP analogs. Like other -glutides, dulaglutide is proven to reduce risk of cardiovascular events. Expect a weight loss of 2.5–4.6 kg (5.5–10 pounds) at the maximum dose of 4.5 mg SC weekly.

Trulicity is supplied in single-dose pens with needle included. The base of the pen is placed against the abdomen and the injection is administered subcutaneously when the green injection button is pushed. The pen is to be kept refrigerated but may be stored at room temperature for up to 14 days.

Dosage adjustment is not necessary with renal or hepatic impairment. Dulaglutide is less likely to cause injection site reactions (0.5%) than most other GLP analogs (although Ozempic is lower at 0.2%).

Dosing: Start 0.75 mg SC once weekly at any time of day, with or without meals. If additional A1C lowering is needed, may increase to 1.5 mg once weekly, 3 mg (after ≥4 weeks on 1.5 mg dose), then 4.5 mg (after ≥4 weeks on 3 mg dose). Max is 4.5 mg weekly.

Dynamic interactions:
- ❖ Glucose lowering

Kinetic interactions:
- ❖ Delayed gastric emptying, otherwise none—"in a bubble"

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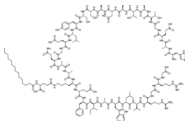
#143
2010
$1,000–$1,220 DM
$1,325–$1,630 weight



Liraglutide (VICTOZA, SAXENDA)

LIR a gloo tide / sax end ah

"Lir's glue tide is a Sax ender"

❖ GLP-1 receptor agonist

Saxenda

FDA-approved for:

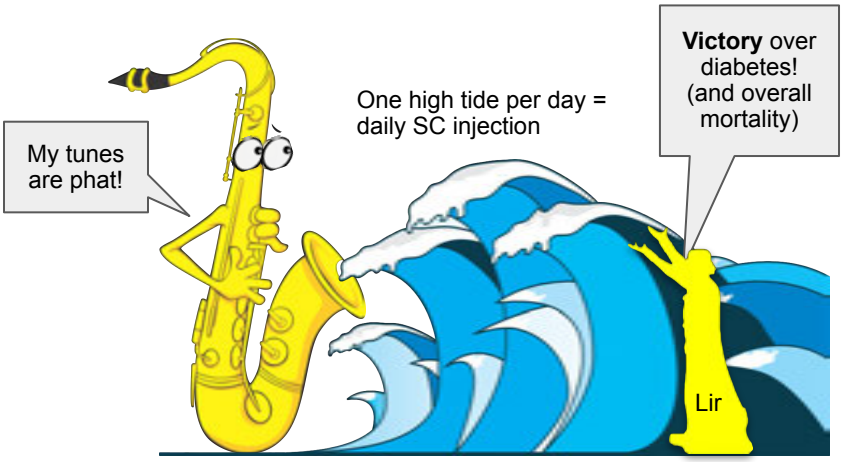
- ❖ Type 2 diabetes (Victoza)
- ❖ Weight management, long-term (Saxenda)

Liraglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist available as a once-daily subcutaneous injectable. It was approved in 2010 for type 2 diabetes as Victoza, and in 2017 for weight loss as Saxenda. Saxenda for weight management is dosed higher (3 mg) than Victoza for diabetes (1.2–1.8 mg). Victoza reduces hemoglobin A1c by about 1.5% and reduces all-cause mortality.

Specifically, Saxenda is indicated for chronic weight management in obese adults (BMI ≥30) or those merely overweight with a BMI ≥27 and a weight-related comorbidity such as hypertension, dyslipidemia, or diabetes.

At doses approved for weight loss, Saxenda is about 50% as effective as Wegovy (semaglutide 2.4 mg SC weekly). At one year, patients on Saxenda had an average placebo-corrected weight loss of 12 pounds or about 6% of body weight. 63% of patients taking Saxenda lost ≥5% body weight. Saxenda should be stopped if loss of body weight <4% after 16 weeks or if the full 3 mg dose is not tolerated.

Saxenda reduces risk of developing type 2 diabetes in individuals taking it for weight loss.



Lir is a sea god in Irish mythology.

Liraglutide formulation	VICTOZA	SAXENDA
	 $1,000–$1,220 monthly at 1.8 mg dose (3 pens)	 $1,325–$1,630 monthly at 3 mg dose (5 pens)
Indication	Type 2 diabetes (age 10+) Cardiovascular event risk reduction in type 2 diabetes	Obesity, long-term treatment
Maintenance dose	1.2–1.8 mg SC daily	3 mg SC daily
Dosing details	Start 0.6 mg SC QD x 1 week (to reduce nausea), then 1.2 mg SC QD. Max is 1.8 mg/day. Administer at any time of day, with or without meals. Retitrate from 0.6 mg if treatment interrupted for >3 days. Only 18 mg pens are available. Dispense 2 pens monthly for 1.2 mg daily dose. Dispense 3 pens monthly for 1.8 mg daily dose. Needles are not included. Compatible with generic insulin pen needles, which come in boxes of 100.	Start 0.6 mg SC daily x 1 week, then increase by 0.6 mg/day in weekly increments to the maintenance dose of 3 mg/day, which is also the maximum dose. Administer at any time of day, with or without meals. Retitrate from 0.6 mg if treatment interrupted for >3 days. Stop Saxenda if weight loss <4% after 16 weeks or if 3 mg dose is not tolerated. At 3 mg/day the pen lasts 6 days, so a month's supply is a carton of 5 pens. Needles are not included. Compatible with generic insulin pen needles, which come in boxes of 100.

When used for diabetes, Victoza has an advantage over other GLP-1 receptor agonists because it is proven to reduce overall mortality—"Victory!". Disadvantages of Victoza include the need for daily injections and a high incidence of nausea (20%).

Victoza lowers hemoglobin A1c by about 1.5%. Incidence of injection site reaction is about 2%, which is more common than with dulaglutide (0.5%) or semaglutide (0.2%).

Dynamic interactions:

- ❖ Glucose lowering

Kinetic interactions:

- ❖ Delayed gastric emptying, otherwise none—"in a bubble"

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2017
$835–$1,020 DM
$8,400– $10,215 weight

Semaglutide (OZEMPIC, RYBELSUS, WEGOVY)

SEM a gloo tide / oh ZEM pick / reb EL sus / wee GOH vee

"Olympic, Rebel, & Wig governor"

❖ GLP-1 receptor agonist

Wegovy

0.25
0.5
1
1.7
2.4 mg

FDA-approved for:

- ❖ Type 2 diabetes (Ozempic, Rybelsus)
- ❖ Weight management, long-term (Wegovy)

Three forms of this GLP analog are available, including the first oral agent in this class, Rybelsus, released in 2019. Original semaglutide, Ozempic, has been available since 2017 for type 2 diabetes. SC Ozempic lowers A1c by 1.0–1.5%. PO Rybelsus is slightly less effective, lowering A1c by about 1.0%.

Wegovy is a high dose formulation of subcutaneous semaglutide approved in 2021 for weight loss—"WE 'gon lose WEight with WEekly WEgovy". Wegovy is indicated for obese patients (BMI >30) or overweight patients with BMI >27 and a weight-related comorbidity.

Wegovy costs ~$9,000 monthly. Copayments are expected to be high. The drug company (Novo Nordisk) offers to reduce copayments to $25 monthly for insured individuals for the first 6 months. GoodRx does not offer much of a discount on Wegovy for the uninsured.

Semaglutide formulation	Dosing	Indication	Dosing	Details
OZEMPIC  $835–$1,020 monthly at 0.5 mg maintenance dose	SC weekly	DM2	Start at 0.25 mg SC weekly at any time of day with or without meals. After 4 weeks, the dose should be increased to the target dose of 0.5 mg weekly. If glycemic control is inadequate, may increase to the maximum dose of 1 mg after at least another 4 weeks. Injected subcutaneously in the abdomen, thigh, or upper arm. Available in two sizes of prefilled multi-dose pens. The 2 mg pen delivers 0.25 mg or 0.5 mg doses. The 4 mg pen delivers four 1 mg doses. Needles are included.	Ozempic lowers A1c by 1.0–1.5%. Lowest risk of injection site reactions among GLP analogs (0.2%). FDA-approved to reduce risk of major cardiovascular events in DM2 patients. Adjustments in dose not necessary for renal or hepatic insufficiency.
RYBELSUS  $835–$1,020 monthly at 7 mg maintenance dose	PO QD	DM2	Start at 3 mg PO QD taken 30 minutes before the first food, drink, or other oral drugs. Swallow the tab with no more than 4 ounces of plain water. After 30 days, increase to the target dose of 7 mg QD. If glycemic control is inadequate, may increase to maximum dose of 14 mg QD after at least 30 days.	Rybelsus lowers A1c by about 1%. Taking the pill <30 minutes before eating can reduce absorption. Waiting longer than 30 minutes to eat (after taking the pill) may increase absorption. Expect a weight loss of 2.5 kg (5.5 pounds).
WEGOVY  $8,400– $10,215 monthly at 2.4 mg maintenance dose	SC weekly	weight	Titrate over 5 months to target dose of 2.4 mg SC weekly. Start at 0.25 mg SC weekly x 4 weeks, then 0.5 mg weekly x 4 weeks, then 1 mg weekly x 4 weeks, then 1.7 mg weekly x 4 weeks, then advance (on month five) to the target dose of 2.4 mg SC weekly. May delay dose titration if gastrointestinal intolerance. Stop Wegovy if 2.4 mg dose is not tolerated. If treatment is interrupted by 2 weeks or longer, retitrate from 0.25 mg. Each pen is single-dose with an integrated needle. Dispense 4 pens per 28 days.	"WE 'gon lose WEight with WEekly WEgovy". Average place-corrected loss of 12% body weight (15% total). Approved for obese patients with BMI >30 or overweight patients with BMI >27 with weight-related comorbidity. Adjustments in dose not necessary for renal or hepatic insufficiency.

Wegovy is the most effective weight loss medication. With Wegovy plus diet and exercise, patients lost an average of about 15% of body weight (12% corrected for placebo). Some subjects lost 20%. Weight loss was stedy for 14 months before plateauing.

Wegovy ($9,000/mo) appears to be about twice as effective as Saxenda (liraglutide), the other GLP analog approved for weight management ($1,500/mo). Semaglutide for weight loss is dosed higher (2.4 mg) than Ozempic for diabetes (0.5–1 mg). Wegovy is more expensive than Ozempic, even on a mg per mg basis. Although not yet approved for weight management, Tirzepatide (Mounjaro) appears to be even more effective for weight loss.

About 7% of participants taking Wegovy dropped out due to adverse events (versus 3% with placebo). Side effects included nausea (44%), vomiting (24%), diarrhea (30%), constipation (24%), abdominal pain (20%), headache (14%), fatigue (11%), dizziness (8%), abdominal distension (7%), and belching (7%).

Semaglutide is the only GLP analog with a warning about diabetic retinopathy, which occured in 4.0% of patients (versus 2.7% with placebo).

Presumably Wegovy can prevent obese patients from developing type 2 diabetes.

Dynamic interactions:

- ❖ Glucose lowering

Kinetic interactions:

- ❖ Delayed gastric emptying, otherwise none—"in a bubble"

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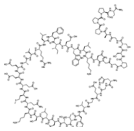
2005
$740–$950 any formulation



Exenatide (BYETTA, BYDUREON)

ex EN a tide / bye A tuh / by DUR ee on

"X in a Tide (Pod)"

❖ GLP-1 receptor agonist

FDA-approved for:
- ❖ Type 2 diabetes

The structure of -**en**atide GLP analogs is based on ex**en**din, a naturally occurring peptide derived from lizard venom. Exendin has 53% homology to human GLP-1. By contrast, the structure of -gl**u**tide GLP analogs is based on h**u**man GLP-1.

The -enatides are short-acting and primarily decrease postprandial (post-meal) blood glucose, with limited impact on fasting glucose. For this reason, they are referred to as prandial GLP-1 receptor agonists. -Enatides slow gastric emptying more prominently than -glutides.

Expected weight loss with the -enatides is only around 3–4 pounds, which is far less than with -glutides. Incidence of injection site reactions is about 4%.

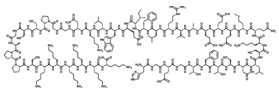
Exenatide, released in 2005 as Byetta, is the oldest GLP analog. Byetta requires BID dosing—"BID-yetta". A weekly formulation of exenatide called Bydureon was approved in 2012. The incidence of injection site reactions with By**dur**eon is about 20%, which is much higher than any other GLP analog—"Your skin better be **dur**able". Byetta has <2% incidence of injection site reactions.

Don't "buy" it.

Glutides are generally preferred over -enatides because -enatides have not been shown to lower the risk of cardiovascular complications such as heart attack and stroke.

Exenatide formulation	**BYETTA**  10 mcg 5 mcg	**BYDUREON**  BCise
Indication	DM2	DM2
Frequency	SC BID	SC weekly
Formulation	60 doses/pen = 30-day supply for 5 mcg/dose or 10 mcg/dose. Needles not supplied with pens.	Single-dose pen or powder for injectable suspension, must be constituted before administration. Single-dose auto-injector is available called Bydureon BCise. 4 pens = 28-day supply.
Dosing	Start with 5 mcg SC BID. May increase to 10 mcg SC BID after one month. Inject within 60 minutes prior to morning and evening meals.	2 mg SC once weekly at any time of day, with or without meals. No titration required due to relatively low incidence of nausea (10%).
Other info	The only GLP analog requiring BID dosing—"BID-yetta"—"Is it injection time **yet**? (probably)". Measured in micrograms instead of milligrams. Not recommended with eGFR <30. Keep refrigerated. Protect from light. After first use, can be kept at room temperature. Discard 30 days after first use.	By**dur**eon (weekly) is more "**dur**able" than Byetta (BID). Measured in milligrams, unlike Byetta. Not recommended with eGFR <45. Exenatide weekly causes the least nausea among GLP analogs. Highest incidence of injection site reactions among GLP analogs, about 20% with either Bydureon formulation.

2016
$690–$710



Lixisenatide (ADLYXIN)

LIX i SEN a tide / ad LIX in

"Add licks in a Tide (Pod)"

❖ GLP-1 receptor agonist

10
20
mcg

FDA-approved for:
- ❖ Type 2 diabetes

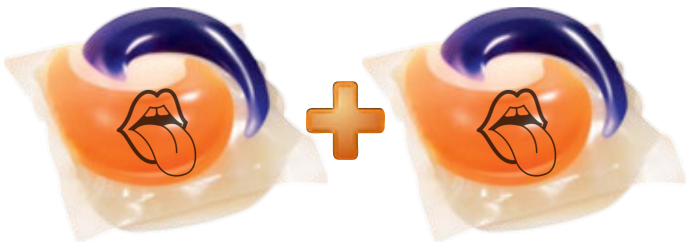
Lixisenatide (Adlyxin) is the newer exendin-based GLP analog. It is not widely prescribed. It is delivered subcutaneously once daily and measured in micrograms.

Pro: Lixisenatide is the only GLP analog that does not have a boxed warning about the risk of thyroid C-cell tumors.

Con: Lixisenatide (daily) is more than twice as likely to cause nausea (25%) than weekly exenatide (Bydureon). -Enatides have not been shown to reduce risk of stroke or myocardial infarction.

A combination product of lixisenatide with insulin glargine (Lantus) is available as SOLIQUA [soh LEE kwa].

Dosing: Start with 10 mcg SC QD for 14 days, then increase to 20 mcg QD. Administer within one hour prior to the first meal of the day. One pen lasts 14 days at the usual adult dosage of 20 mcg.



Dynamic interactions:
- ❖ Glucose lowering

Kinetic interactions:
- ❖ Delayed gastric emptying, otherwise none—"in a bubble"

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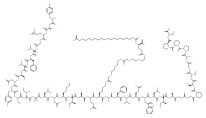
2022
$1060



Tirzepatide (MOUNJARO)

tir ZEP a tide / mown JAHR OH

"Tear zeppelin (over) Mount (Kiliman)jaro"

Dual GLP-1/GIP receptor agonist

2.5
5
7.5
10
12.5
15 mg

FDA-approved for:
- ❖ Type 2 diabetes

Used off-label for:
- ❖ Weight management

Tirzepatide (Mounjaro) is the first "twincretin" for type 2 diabetes. It is a GLP-1 agonist like the other medications in this chapter, and also a glucose-dependent insulinotropic polypeptide (GIP) agonist. GIP is similar to GLP-1. Both are secreted in the gut in response to food.

Tirzepatide is injected subcutaneously on a monthly basis.

It appears to be superior to all predecessors in magnitude of weight gain and hemoglobin A1c reduction. It has not (yet) been approved for weight management.

Tirzepatide (when added to metformin) can reduce A1c by up to 2.3%. It can lead to weight loss of up to 25 pounds over 10 months in patients with diabetes.

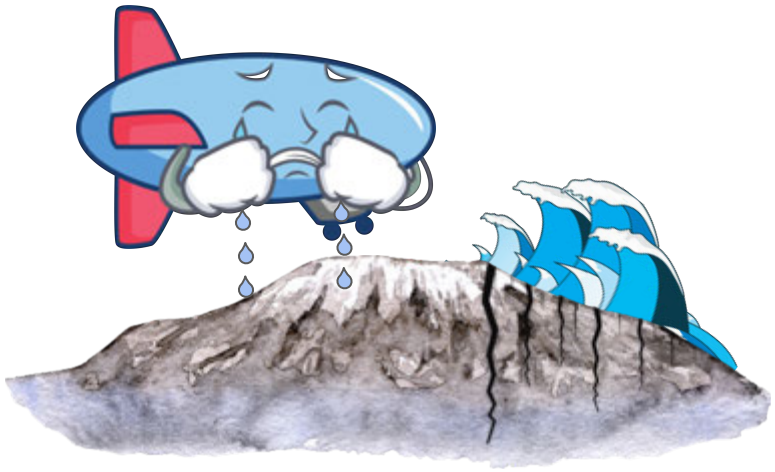
Over 72 weeks patients without diabetes lost 15%, 19%, and 21% of body weight on the 5, 10, and 15 mg weekly SQ injections, respectively. About 90% of those who received the 10- or 15-mg dose achieved ≥5% weight loss.

Data on whether tirzepatide lowers cardiovascular outcomes is not expected until 2025.

The most common side effects are nausea (~15%), diarrhea (~15%), and other gastrointestinal complaints.

Cautions applicable to other GLP-1 agonists apply to tirzepatide. Serious hypersensitivity reactions such as anaphylaxis and angioedema have occurred with these drugs. It is contraindicated for use in patients with a personal or family history of medullary thyroid carcinoma and in those with multiple endocrine neoplasia type 2.

The label cautions about possible reduced efficacy of oral contraceptives due to delayed gastric emptying. Women of childbearing potential taking an oral hormonal contraceptive should add a barrier contraceptive for 4 weeks after starting tirzepatide and after each dose escalation.



Dosing: Start 2.5 mg injected SQ once weekly in the abdomen, thigh, or upper arm. After 4 weeks, the dose should be increased to 5 mg. If additional glycemic control is needed, the dose can be increased in 2.5-mg increments every 4 weeks to a maximum of 15 mg once weekly.

Dynamic interactions:
- ❖ Glucose lowering

Kinetic interactions:
- ❖ Delayed gastric emptying, otherwise none—"in a bubble"

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