



The GLP-1 Playbook: Smarter Strategies for Diabetes Management

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Disclosures:

Emily Eddy reports she has no relevant financial relationships to disclose.

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Identify appropriate patient populations for GLP-1 therapy based on current guidelines, comorbidities, and individualized treatment goals.

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Analyze real-world patient cases to identify opportunities to optimize patient care plans and support services related to GLP-1 receptor agonist therapy.

Abbreviations

A1c = Hemoglobin A1c

ASCVD = AtheroSclerotic CardioVascular Disease

BG = Blood Glucose

CKD = Chronic Kidney Disease

CV = Cardiovascular

CVD = Cardiovascular Disease

GIP = Glucose-dependent insulintropic polypeptide

GLP-1 RA = glucagon-like peptide -1 receptor agonist

HbA1c= Hemoglobin A1c

HTN = hypertension

MACE = Major Adverse Cardiovascular Event

MASH= Metabolic Dysfunction-Associated
Steatohepatitis

SGLT2= Sodium-Glucose Co-Transporter 2

OSA= Obstructive Sleep Apnea

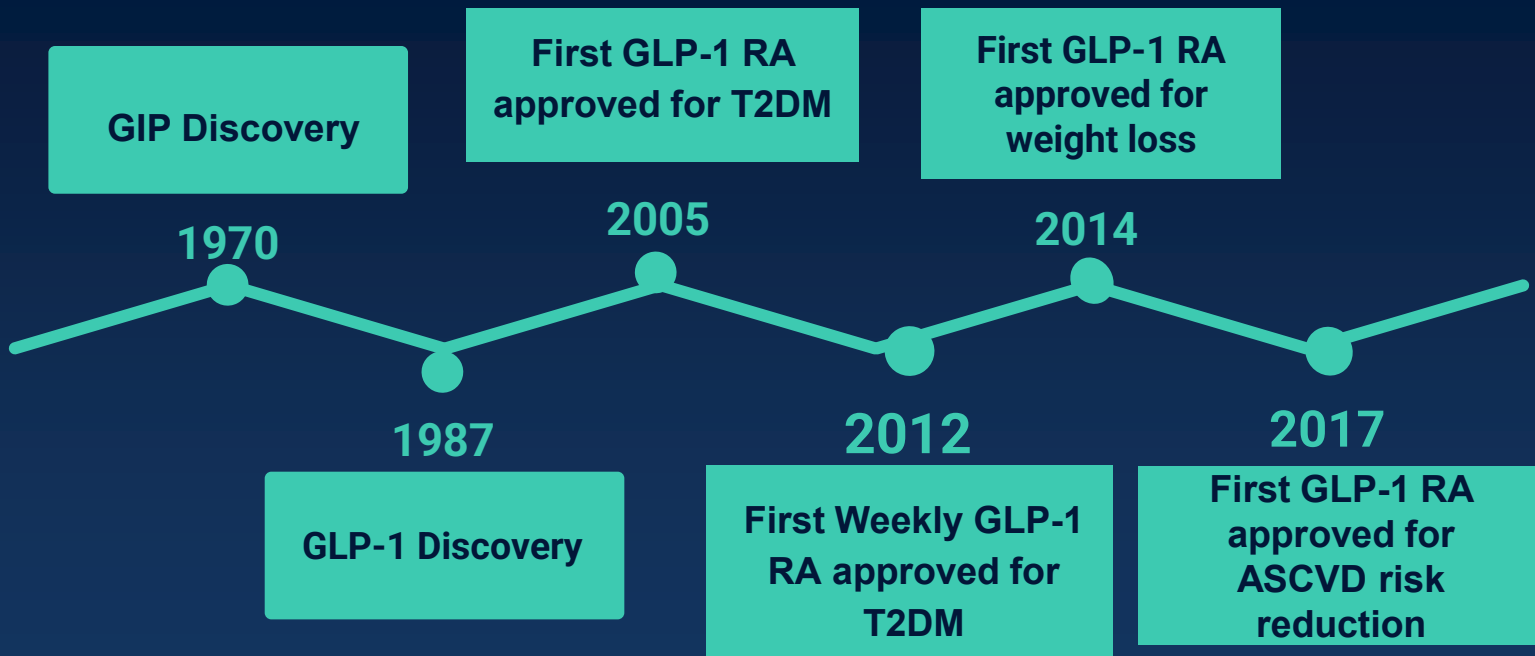
T2DM = type 2 diabetes



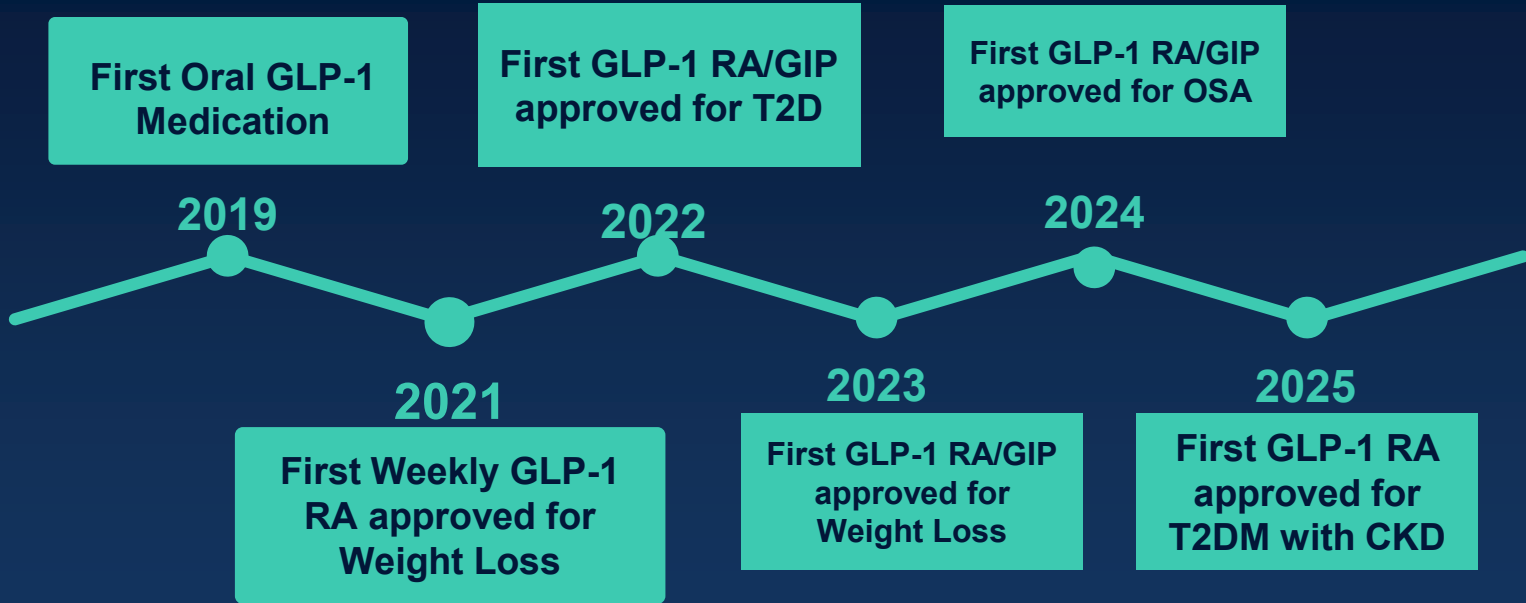
01.

- Mechanism of action
- Pharmacologic differences
- Clinical benefits of GLP-1 receptor agonists

Incretin Therapy Timeline



Incretin Therapy Timeline



How Do They Work?

Comparison of Proposed Actions of GIP And GLP-1⁵



Brain

GIP Activity

- Reduced food intake

GLP-1 Activity

- Reduced food intake
- Increased satiety



Whole-Body

GIP Activity

- Increased insulin sensitivity



Pancreas

GIP Activity

- Increased insulin
- Increased glucagon

GLP-1 Activity

- Increased insulin
- Reduced glucagon



Stomach

GLP-1 Activity

- Reduced gastric emptying

GLP-1 RA and GLP-1 RA/GIP Indications

Current FDA Indications

- Type 2 Diabetes
- Type 2 Diabetes and CKD
- Weight Loss
- Atherosclerotic Cardiovascular Disease (ASCVD)
- Metabolic Dysfunction-Associated Steatohepatitis (MASH)

Potential Indications*

- Substance Use Disorder
- Alzheimer's Disease
- Osteoarthritis
- Asthma
- Rheumatoid Arthritis
- Parkinson's Disease

- And MORE!

Benefits of GLP-1 and GLP-1RA/GIP

A1C Lowering

Weight Loss

ASCVD Benefit*

CKD Benefit*

Liver Health Improvement

BP Lowering, Obstructive Sleep Apnea, Osteoarthritis, Substance Use?,

Side Effects and Warnings with GLP-1 RA or GLP-1 RA/GIP

Nausea and vomiting

Constipation

Multiple Endocrine Neoplasia syndrome type 2 (MEN 2)

Pancreatitis

Medullary Thyroid Carcinoma (MTC)



02.

- Compare GLP-1 Products

Available Products

Indicated for Diabetes				
Product	Dosage Form	Available Strengths	Route	Frequency
GLP-1 RA				
dulaglutide (Trulicity®)	pen injector	0.75 mg, 1.5 mg, 3 mg, 4.5 mg / 0.5 mL	SQ	Weekly
exenatide ER (Bydureon BCise®)	auto-injector	2 mg / 0.85 mL	SQ	Weekly
exenatide IR (Byetta™)	pen injector	5 mcg / 0.02 mL, 10 mcg / 0.04 mL	SQ	Twice Daily
liraglutide (Victoza®)	pen injector	18 mg / 3 mL	SQ	Daily
semaglutide (Ozempic®)	pen injector	2 mg, 4 mg, 8 mg / 3 mL	SQ	Weekly
semaglutide (Ozempic®)	tablet	1.5 mg, 4 mg, 9 mg	oral	Daily
semaglutide (Rybelsus®)	tablet	3 mg, 7 mg, 14 mg	oral	Daily
GIP / GLP-1 RA				
tirzepatide (Mounjaro®)	pen injector	2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg / 0.5 mL	SQ	Weekly

Oral Semaglutide

- New Formulation
 - Specific tablet design and absorption enhancer



Sip

Take the pill when you wake up, first thing in the morning, on an empty stomach, with a small sip of water (up to 4 ounces).



Go

Start your morning. Wait at least 30 minutes before eating, drinking, or taking other oral medications.

A1C

Meta-Analysis of GLP-1 RA and GLP-1 RA/GIP 2021

Tirzepatide produced greater HbA1c reductions than GLP-1 RAs.

HbA1c reduction versus GLP-1 RAs ranged from:

- **-0.29% to -0.92% additional lowering**
depending on tirzepatide dose

Meta-Analysis of GLP-1 RA and GLP-1 RA/GIP 2024

Key findings:

- Tirzepatide ranked highest for HbA1c reduction.
- Mean HbA1c reduction:
 - **Tirzepatide: -2.10%**
 - Greater than semaglutide, dulaglutide, liraglutide, and other GLP-1 RAs.

Weight Loss

Agent	Typical Weight Loss
liraglutide 1.8 mg	2 - 4 kg
dulaglutide	2 - 5 kg
semaglutide 1 mg	4 - 6 kg
semaglutide 2 mg	6 - 7 kg
semaglutide 2.4 mg	~13.7 %
tirzeptide 15 mg	~21 %

SURPASS-2 Trial

Outcome	Tirzepatide 5 mg	Tirzepatide 10 mg	Tirzepatide 15 mg	Semaglutide 1 mg
HbA1c Change	-2.09%	-2.37%	-2.46%	-1.86%
Weight Change	-7.8 kg	-10.3 kg	-12.4 kg	-6.2 kg
Achieved HbA1c <7%	85%	89%	92%	81%
Achieved HbA1c <5.7%	29%	45%	51%	20%

ASCVD

(Bu, 2024), (Kotecha, 2025), (Medhi, 2023) (ADA standard 10, 2026)

Improve Cardiometabolic Risk Factors

- **Lower A1C** and improve glycemic control
- **Promote weight loss**, especially visceral fat reduction
- **Reduce blood pressure**
- **Improve lipid profile** (↓ triglycerides, modest LDL improvement)

Reduce Vascular Damage

- **Decrease systemic inflammation**
- **Improve endothelial function**
- **Slow atherosclerotic plaque progression**

Improve Cardiovascular Outcomes

- ↓ Major adverse cardiovascular events (MACE)
- ↓ Myocardial infarction (heart attack)
- ↓ Stroke
- ↓ Cardiovascular mortality

ASCVD

FDA Indications

- semaglutide
- dulaglutide
- liraglutide
- oral semaglutide

Shown ASCVD Benefit

- tirzepatide

CKD

Reduces inflammation and fibrosis

- Decreases renal inflammation and oxidative stress
- Limits kidney scarring and structural damage

Improve glycemic control:

- Lowers blood glucose through glucose-dependent insulin secretion
- Reduces risk of hypoglycemia, even in patients with CKD

Reduce intraglomerular pressure and hyperfiltration:

- Promotes natriuresis and improves kidney hemodynamics
- Helps slow progression of CKD

The FLOW Trial: semaglutide

About

Phase 3 double-blind controlled
240 weeks

Patients:
T2DM and CKD

semaglutide 1 mg
vs. placebo

Clinical Efficacy

Primary outcome:

- **Reduced risk of major kidney events:** Semaglutide lowered the risk of the primary composite kidney outcome (persistent $\geq 50\%$ eGFR decline, kidney failure, or kidney/CV death) with a 24% relative risk reduction compared with placebo (HR 0.76; 95% CI, 0.66–0.88; $P = 0.0003$).
- **Slowed kidney function decline:** Semaglutide slowed the annual loss of eGFR compared with placebo, with a mean difference of ~ 1.16 mL/min/1.73 m² per year in favor of semaglutide.

Key Point

patients with T2DM and CKD, semaglutide significantly reduced major kidney outcomes and slowed eGFR decline

Side Effects

Adverse Effect	semaglutide	dulaglutide	liraglutide	tirzepatide
Nausea	15-44%	12-21%	20-40%	18-32%
Vomiting	5-24%	6-13%	8-20%	6-18%
Constipation	5-24%	3-7%	8-20%	11-21%
Injection Side Reactions	< 5%	1-5%	2-10%	< 5%
Treatment Discontinuation	3-8%	2-6%	4-10%	4-8%



03.

- Patients Indicated for GLP-1 Therapy

What Does the ADA Say?

9.7

In adults with type 2 diabetes and established or high risk of **atherosclerotic cardiovascular disease**, the treatment plan should include medications with demonstrated benefits to reduce cardiovascular events (e.g., glucagon-like peptide 1 receptor agonist [GLP-1 RA] ...) for glycemic management and comprehensive cardiovascular risk reduction (irrespective of A1C)

9.9a

In adults with type 2 diabetes, obesity, and symptomatic heart failure with **preserved ejection fraction (HFpEF)**, the glucose-lowering treatment plan should include a dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 RA with demonstrated benefits for HF-related symptoms and reduction in HF events (irrespective of A1C).

9.10

In adults with type 2 diabetes who have **chronic kidney disease (CKD)** (with confirmed estimated glomerular filtration rate eGFR 20–60 mL/min/1.73 m² and/or albuminuria), an SGLT2 inhibitor or GLP-1 RA with demonstrated benefit in this population should be used for both glycemic management and for slowing progression of CKD and reduction in cardiovascular events (irrespective of A1C)

What Does the ADA Say?

9.12

In adults with type 2 diabetes, **metabolic dysfunction–associated steatotic liver disease (MASLD)**, and overweight or obesity, consider using a GLP-1 RA with demonstrated benefits in metabolic dysfunction–associated steatohepatitis (MASH) or a dual GIP and GLP-1 RA with potential benefits in **MASH** for glycemic management and as an adjunctive therapy to interventions for weight loss.

9.22

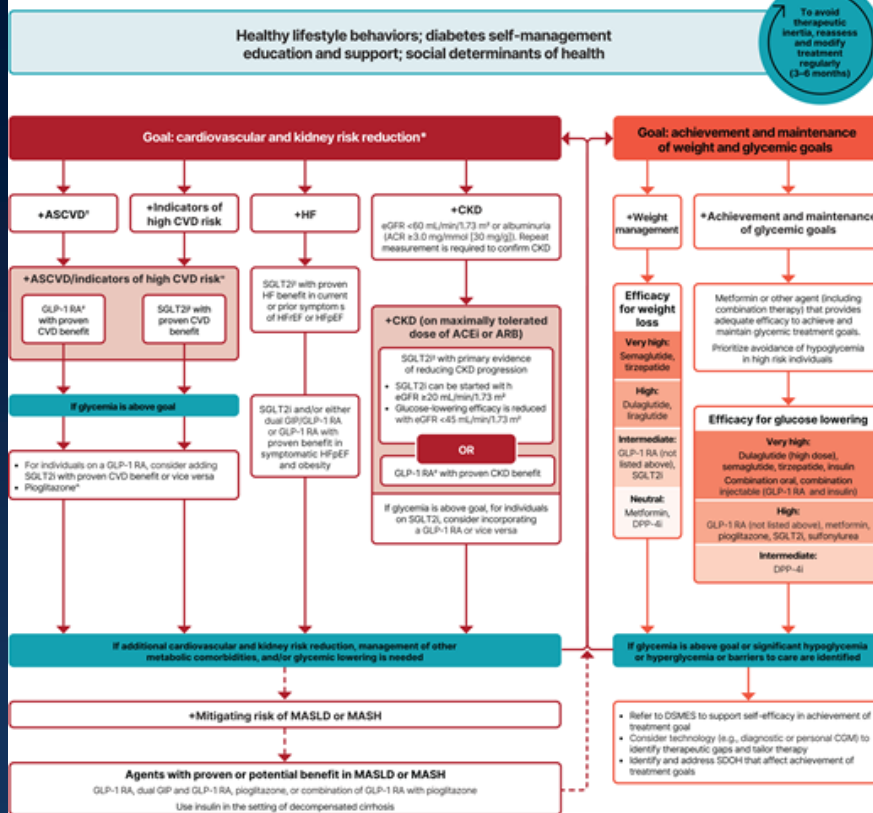
If **insulin is used**, combination therapy with a GLP-1 RA, including a dual GIP and GLP-1 RA, is recommended for greater glycemic effectiveness as well as beneficial effects on weight and hypoglycemia risk for adults with type 2 diabetes. Insulin dosing should be reassessed upon addition or dose escalation of a GLP-1 RA or dual GIP and GLP-1 RA.

9.10

Apply obesity management strategies used in the general adult population, including GLP-1 RA–based therapy and metabolic surgery, to adults with **type 1** diabetes who have obesity (BMI ≥ 30.0 kg/m², or ≥ 27.5 kg/m² in Asian American individuals)

Use of glucose-lowering medications in the management of type 2 diabetes

(For recommendations for specific conditions, including non-glucose-lowering medications, refer to pertinent sections)



* In people with HF, CKD, established CVD, or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be made irrespective of attainment of glycemic goal.

† ASCVD Defined differently across CVDt's but all included individuals with established CVD (e.g., MI, stroke, and arterial revascularization procedure) and variably included conditions such as transient ischemic attack, unstable angina, amputation, and symptomatic or asymptomatic coronary artery disease. Indicators of high risk: While definitions vary, most comprise ≥ 55 years of age with two or more additional risk factors (including obesity, hypertension, smoking, dyslipidemia, or albuminuria).

* A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high risk CVD. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details.

† For GLP-1 RAs, CVDt's demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and kidney end points in individuals with T2D with established or high risk of CVD. One kidney outcome trial demonstrated benefit in reducing persistent eGFR reduction and CV death for a GLP-1 RA in individuals with CKD and T2D.

‡ For SGLT2is, CV and kidney outcomes trials demonstrate their efficacy in reducing the risks of composite MACE, CV death, all-cause mortality, MI, HF, and kidney outcomes in individuals with T2D and established or high risk of CVD.

* Low-dose pioglitazone may be better tolerated and similarly effective as higher doses.



04.

- Therapy Optimization
- Patient Case

Frequently Asked Questions

1. How do you prevent or minimize some of the side effects of GLP-1 Therapy?
2. What are important nutrition counseling recommendations for patients on these medications?
3. How do you handle missed dosing?
4. How do you switch between products?
5. What about microdosing or extended interval dosing?

How do you prevent or minimize some of the side effects of GLP-1 therapy?

1. Eating habits



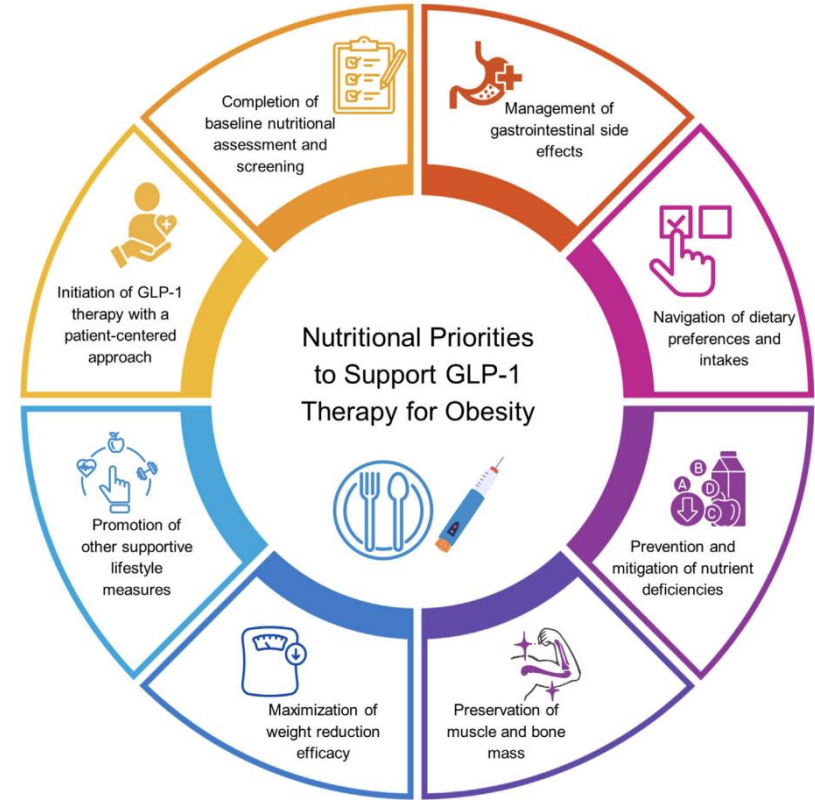
2. Food composition



3. Lifestyle



What are important nutrition counseling recommendations for patients on these medications?



How do you handle missed dosing?

Medication	Recommended Dosing Interval	Manufacturer Recommendations for Missed Doses
exenatide ER	Once Weekly	Administer as soon as possible if there are ≥ 3 days until the next scheduled dose. If not then skip the dose and administer it on the next scheduled day.
dulaglutide	Once Weekly	Administer as soon as possible if there are ≥ 3 days until the next scheduled dose. If not then skip the dose and administer it on the next scheduled day.
liraglutide	Once Daily	If a dose is missed, resume the once-daily regimen as prescribed with the next scheduled dose. Do not administer an extra dose or increase in dose to make up for the missed dose.
semaglutide (SQ)	Once Weekly	Administer as soon as possible within 5 days of a missed dose. If > 5 days have passed, skip the dose and administer it on the next day the dose is due.
semaglutide (oral)	Once Daily	If a dose is missed, resume the once-daily regimen as prescribed with the next scheduled dose.
tirzepatide	Once Weekly	Administer as soon as possible within 4 days after the missed dose. If > 4 days have passed, skip the dose and administer it on the next scheduled day.

ER: extended-release; SQ: subcutaneous

How do you switch between products?

Agent	Dosing Route and Interval						
liraglutide	SC daily	0.6 mg	1.2 mg	1.8 mg			
exenatide ER	SC weekly			2 mg			
dulaglutide	SC weekly		0.75 mg	1.5 mg	3 mg- 4.5 mg		
semaglutide	SC weekly		0.25 mg	0.5 mg	1 mg	2 mg	
semaglutide	PO daily	3 mg	7 mg	14 mg			
tirzepatide	SC weekly				2.5 mg*	5 mg	7.5 mg-15 mg

ER: extended release; PO: by mouth; SC: subcutaneous

What about microdosing or extended interval dosing?

Microdosing (Lower Doses)

- Off-label practice of using doses lower than the initial starting dose
 - (e.g., <0.25 mg semaglutide).
- Aim: Mitigate extreme GI sensitivity or "brain fog" reported by some patients.
- Lack of clinical trial data to support efficacy for A1C or weight goals.

Extended Interval Dosing

- Spacing doses further apart (e.g., every 10–14 days) during shortages or maintenance.
- Aim: Maintain weight loss while reducing side effects or stretching supply.
- Risk: Potential loss of glycemic control and GI intolerance when resuming regular schedule.

Clinical Implications & Best Practices:

- Titration is key: Standard protocols are designed to build tolerance.
- Shortage Management: Extended intervals may be necessary but require close BG monitoring.
- Patient Counseling: Caution patients against self-adjusting doses without provider oversight.

Patient Case

ML (55 yo WF) Presents for Diabetes Management

Setting the Scene:

Pt is seeing you today because they are interested in starting a GLP-1 RA and they are nervous and need some help and guidance with medications.

Symptoms/History:

- She wears her CGM and reports frequent hypoglycemia overnight and mid-afternoon
- She has a BMI of 36 and reports desiring to lose weight
- Not currently following any diet but reports having a very “sensitive stomach”

- T2DM x 12 years
- HTN x 10 years
- HLD x 10 years
- Depression x 20 years
- CKD x 6 years

Medications:

- **metformin** 1000 mg BID
- **insulin glargine** 24 units daily
- **insulin lispro** 6-10 units with meals
- **lisinopril** 20 mg daily
- **atorvastatin** 20 mg daily
- **sitagliptin** 100 mg daily
- **sertraline** 50 mg daily
- **CGM** as directed

Labs Provided by ML:

- A1C is 8.6%

Key Takeaways: GLP-1 Therapy Optimization

Clinical Superiority

- Tirzepatide demonstrates the greatest reductions in both HbA1c (-2.10%) and body weight (~21%) compared to other GLP-1 RAs.
- Dual GIP/GLP-1 agonism produces synergistic metabolic benefits.

Cardio-Renal Protection

- GLP-1 RAs are "cardio-renal-metabolic" drugs with proven ASCVD and CKD benefits.
- Semaglutide significantly reduces major kidney outcomes and slows eGFR decline.

Practical Implementation

- Titration is critical to mitigate GI side effects like nausea and vomiting.
- ADA 2026 Standards recommend use of GLP-1 RA or GLP-1 RA/GIP in many patients but they don't come without risks
- Pharmacists/Pharmacy Technicians play an important role in proper usage of these medications

Knowledge Checks

Question #1

Which of the following GLP-1 RA agents is ranked highest for mean HbA1c reduction, according to the 2024 meta-analysis?

- a. dulaglutide
- b. liraglutide
- c. semaglutide
- d. tirzepatide

Question #2

Which of the following is a current FDA indication for a GLP-1 RA or GLP-1 RA/GIP medication?

- a. Substance Abuse
- b. Chronic Kidney Disease (CKD)
- c. Osteoarthritis
- d. Alzheimer's Disease

Question #3

When implementing GLP-1 RA therapy, what is identified as a critical best practice to mitigate GI side effects like nausea and vomiting?

- a. Extended Interval Dosing
- b. Titration
- c. Microdosing
- d. Daily blood glucose monitoring

Question #4

Which best describes a primary mechanism of GLP-1 receptor agonists?

- A. Increased insulin resistance in peripheral tissues
- B. Glucose-dependent stimulation of insulin secretion and delayed gastric emptying
- C. Inhibition of SGLT2 receptors in the renal tubule
- D. Direct stimulation of pancreatic alpha-cell glucagon release

Question #5

A patient misses their weekly GLP-1 RA dose by 4 days. What should the pharmacist advise (for once-weekly semaglutide)?

- a. Skip the dose entirely
- b. Take the dose as soon as possible
- c. Take two doses the next week
- d. Restart titration from the beginning

References

- Alenezi F, Alshamrani M, Alshammari K, et al. The effect of GLP-1 receptor agonists on renal outcomes: a systematic review and meta-analysis. *Nephrol Dial Transplant*. 2025. Published online August 2025. doi:10.1093/ndt/gfaf291.
- American Diabetes Association Professional Practice Committee for Diabetes. 8. Obesity and weight management for the prevention and treatment of diabetes: Standards of Care in Diabetes—2026. *Diabetes Care*. 2026;49(suppl 1):S166-S182. doi:10.2337/dc26-S008.
- American Diabetes Association Professional Practice Committee for Diabetes. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes—2026. *Diabetes Care*. 2026;49(suppl 1):S183-S215. doi:10.2337/dc26-S009.
- Bu T, Sun Z, Pan Y, Deng X, Yuan G. Glucagon-Like Peptide-1: New Regulator in Lipid Metabolism. *Diabetes Metab J*. 2024;48(3):354-372. doi:10.4093/dmj.2023.0277.
- Dulaglutide. In: *Lexicomp Online*. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. Updated May 14, 2026. Accessed June 1, 2026.
- Eddy E, Long B. *Navigating the Storms: GLP-1 RAs and GIP/GLP-1 RAs Management and Best Practices*. Ohio Pharmacists Association; 2024. 1.5 CEU Continuing Education.
- Exenatide. In: *Lexicomp Online*. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. Updated May 23, 2026. Accessed June 1, 2026.
- 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.
- Gorgojo-Martínez JJ, Mezquita-Raya P, Carretero-Gómez J, Castro A, Cebrián-Cuenca A, de Torres-Sánchez A, García-de-Lucas MD, Núñez J, Obaya JC, Soler MJ, Górriz JL, Rubio-Herrera MÁ. Clinical recommendations to manage gastrointestinal adverse events in patients treated with GLP-1 receptor agonists: a multidisciplinary expert consensus. *J Clin Med*. 2023;12(1):145. doi:10.3390/jcm12010145.
- Hoog MM, Vallarino C, Maldonado JM, Grabner M, Teng CC, Terrell K, Richard EL. Real-world effectiveness of tirzepatide versus semaglutide on HbA1c and weight in patients with type 2 diabetes. *Diabetes Ther*. 2025;16(11):2237-2256. doi:10.1007/s13300-025-01794-9.

References

- Jastreboff AM, Aronne LJ, Ahmad NN, et al. Tirzepatide once weekly for the treatment of obesity. *N Engl J Med*. 2022;387(3):205-216. doi:10.1056/NEJMoa2206038.
- Karagiannis T, Avgerinos I, Liakos A, Del Prato S, Matthews DR, Tsapas A, Bekiari E. Management of type 2 diabetes with the dual GIP/GLP-1 receptor agonist tirzepatide: a systematic review and meta-analysis. *Diabetologia*. 2022;65(8):1251-1261. doi:10.1007/s00125-022-05715-4.
- Kotecha P, Huang W, Yeh YY, et al. Efficacy and safety of GLP-1 receptor agonists in children and adolescents with obesity or type 2 diabetes. *JAMA Pediatr*. 2025;179(12):1308-1317. doi:10.1001/jamapediatrics.2025.3243.
- Liraglutide. In: *Lexicomp Online*. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. Updated May 29, 2026. Accessed June 1, 2026.
- Mann JFE, Rossing P, Bakris G, et al. Effects of semaglutide with and without concomitant SGLT2 inhibitor use in participants with type 2 diabetes and chronic kidney disease in the FLOW trial. *Nat Med*. 2024;30(10):2849-2856. doi:10.1038/s41591-024-03133-0.
- Mehdi SF, Pusapati S, Anwar MS, Lohana D, Kumar P, Nandula SA, Nawaz FK, Tracey K, Yang H, LeRoith D, Brownstein MJ, Roth J. Glucagon-like peptide-1: a multi-faceted anti-inflammatory agent. *Front Immunol*. 2023;14:1148209. doi:10.3389/fimmu.2023.1148209.
- Mozaffarian D, Agarwal M, Aggarwal M, Alexander L, Apovian CM, Bindlish S, et al. Nutritional priorities to support GLP-1 therapy for obesity: a joint advisory from the American College of Lifestyle Medicine, the American Society for Nutrition, the Obesity Medicine Association, and The Obesity Society. *Am J Clin Nutr*. 2025;122(1):344-367. doi:10.1016/j.ajcnut.2025.04.023.
- Semaglutide. In: *Lexicomp Online*. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. Updated May 21, 2026. Accessed June 1, 2026.
- Tirzepatide. In: *Lexicomp Online*. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. Updated May 29, 2026. Accessed June 1, 2026.
- Tuttle KR, Mann JFE, Mayrdorfer MM, et al; FLOW Trial Investigators. Kidney and survival outcomes with semaglutide by CKD severity in the FLOW trial. *Clin J Am Soc Nephrol*. 2026;21(5):841-851. doi:10.2215/CJN.0000000974.
- Yao H, Zhang A, Li D, Wu Y, Wang CZ, Wan JY, Yuan CS. Comparative effectiveness of GLP-1 receptor agonists on glycaemic control, body weight, and lipid profile for type 2 diabetes: systematic review and network meta-analysis. *BMJ*. 2024;384:e076410. doi:10.1136/bmj-2023-076410.