Women's Health 2024 | Beyond the Annual Visit

GLP-1 Receptor Agonists: Managing the Hype and the Hope

Amy L. Clouse, MD

Associate Clinical Professor, Family and Community Medicine
Sidney Kimmel Medical College, Thomas Jefferson University
Associate Director, Family Medicine Residency Program
Jefferson–Abington Health

Learning Objectives

1

Understand the mechanism of action of GLP-1 and the similarities and differences among the available glucagon-like peptide-1 receptor agonists (GLP-1 RAs)

2

Select GLP-1 RAs based on the updated ADA guidelines for T2DM medication management, integrating patient comorbidities and considerations

3

Individualize treatment plans using the GLP-1 RAs with attention to common patient questions and concerns, including drug shortages

Learning Objectives

1

Understand the mechanism of action of GLP-1 and the similarities and differences among the available glucagon-like peptide-1 receptor agonists (GLP-1 RAs)

Native GLP-1 and GIP Actions

GLP-1 and GIP released from small intestine

Native GLP-1 and GIP Actions

In T2DM, there is an impaired insulin response to GLP-1, possibly related to reduced postprandial GLP-1 secretion

GLP-1 and GIP released from small intestine

Slow gastric emptying

Regulate appetite

Promote insulin and decrease glucagon secretion

Increase diuresis and renal blood flow

Decrease glucose production

Improve endothelial function
Decrease inflammation

Drucker DJ. *Cell Metab*. 2016;24(1):15-30.
Nauck MA, et al. *Diabetes Obes Metab*. 2021;23 Suppl 3:5-29.

Synthetic GLP-1 RAs and GLP-1/GIP

- Longer half-life than endogenous GLP-1
  - Resistant to degradation by enzyme DPP-4
- Can be administered once daily or once weekly
- Bind to the GLP-1 receptor and stimulate glucose-dependent insulin release from the pancreatic islet cells

Side Effects

Gastrointestinal –
up to 50% in clinical trials[1,2]

- Nausea
- Vomiting
- Diarrhea
- Constipation

Gallbladder

- Increased risk of cholelithiasis and cholecystitis; no causal relationship identified but FDA includes as a warning for all GLP-1 RAs[3]

Pancreas

- Pancreatitis has been reported but insufficient data to establish causal relationship; no association between GLP-1 RAs and increased risk of acute pancreatitis or pancreatic cancer seen in CVOT trial data[4]

Hypersensitivity

- Injection site reactions ~10%[5]

1. Shyangdan DS, et al. *Cochrane Database Syst Rev*. 2011;2011(10):CD006423. 2. Sodhi M, et al. *JAMA*. 2023;330(18):1795-1797. 3. Woronow D, et al. *JAMA Intern Med*. 2022;182(10):1104-1106. 4. He L, et al. *JAMA Intern Med*. 2022;182(5):513-519. 5. Rosenstock J, et al. *Diabetes Care*. 2014;37(8):2317-2325.

FDA-Approved GLP-1 Receptor Agonists

GLP-1 Receptor Agonists:

- Exenatide
- Lixisenatide*
- Liraglutide
- Dulaglutide
- Semaglutide

*Lixisenatide is no longer available in the US as an individual agent, only in combination with insulin glargine as Soliqua daily injection

GLP-1/GIP Receptor Agonist:
Tirzepatide

In Development:

- New GLP-1 RA: **Efpeglenatide**
- Triple-acting GLP-1/GIP/glucagon RA: **Retatrutide**
- Non-peptide oral GLP-1 RAs:
  - **Danuglipron**
  - **Orforglipron**

Dosing and Delivery Devices for Available GLP-1 RAs and a GLP-1 RA/GIP

GLP-1 RA	Brand Name	How Dosed	How Supplied	Dosing
Liraglutide	Victoza	Daily SC Injection	Multidose pens with pen needles*	0.6, 1.2, or 1.8 mg from same pen
	Saxenda	Daily SC Injection	Multidose pens with pen needles*	As above but also 0.24 and 3.0 mg
Exenatide	Byetta	BID SC Injection	Multidose pens with pen needles*	5 mcg and 10 mcg pens
	Bydureon BCise	Weekly SC Injection	Single-use prefilled autoinjector pens	2 mg pen
Dulaglutide	Trulicity	Weekly SC Injection	Single-use prefilled autoinjector pens	0.75, 1.5, 3.0, and 4.5 mg pens
Semaglutide	Rebelsus	Daily Pill	Oral Tablet	3 mg, 7 mg, 14 mg tablets
	Ozempic	Weekly SC Injection	Multidose or single-use prefilled pens with pen needles*	0.25/0.5 mg from same pen or 1 mg or 2 mg from single-use pen
	Wegovy	Weekly SC Injection	Single-use prefilled autoinjector pens	0.25, 0.5, 1.0, 1.7, or 2.4 mg pens
GLP-1 RA/GIP				
Tirzepatide	Mounjaro	Weekly SC Injection	Single-use prefilled autoinjector pens	2.5, 5.0, 7.5, 10, 12.5, 15 mg pens
	Zepbound	Weekly SC Injection	Single-use prefilled autoinjector pens	Same as above

* Separate Rx.
From prescribing information from each manufacturer's website, accessed individually on 8/17/24.

Weight Loss and Glucose-Lowering Efficacy

in Patients With T2DM and/or Obesity

Semaglutide[1-3]		
Dose	**Δ HbA1c**	**Weight Loss**
14 mg PO	-1.4%	-8.2 lbs
2 mg SC	-2.1%	-14.2 lbs (also on metformin +/- sulfonylurea)
2.4 mg SC	na	-9.6% body wt (pts w/ overweight/obesity)

Tirzepatide[4,5]		
15 mg	-1.7%	-17.2 lbs
15 mg	na	-14.7% body wt (pts w/ overweight/obesity)

Dulaglutide[6-8]		
Dose	**Δ HbA1c**	**Weight Loss**
4.5 mg	-1.8%	-10.4 lbs (also on metformin)

Liraglutide[9,10]		
1.8 mg	-1.1%	-5.5 lbs
3 mg	na	-5.4 lbs (pts w/ overweight/obesity)

1. Ozempic. Prescribing information. Novo Nordisk Inc; 2022. 2. Wegovy. Prescribing information. Novo Nordisk Inc; 2022. 3. Rybelsus. Prescribing information. Novo Nordisk Inc; 2023. 4. Mounjaro. Prescribing information. Eli Lilly and Company; 2023. 5. Garvey WT, et al. *Lancet*. 2023;402(10402):613-626. 6. Trulicity. Prescribing information. Eli Lilly and Company; 2022. 7. Bonora E, et al. *Diabetes Obes Metab*. 2021;23(10):2242-2250. 8. Frias JP, et al. *Diabetes Care*. 2021;44(3):765-773. 9. Victoza. Prescribing information. Novo Nordisk Inc; 2022. 10. Saxenda. Prescribing information. Novo Nordisk Inc; 2022.

Cardiovascular Outcomes Trials for GLP-1 RAs

Major adverse cardiovascular events: MI, stroke, CV death	**Liraglutide** (Victoza) LEADER[1]	**Exenatide ER** (Bydureon) EXSCEL[2]	**Dulaglutide** (Trulicity) REWIND[3]	**Oral Semaglutide** (Victoza) PIONEER 6[4]	**SC Semaglutide** (Ozempic/Wegovy) SUSTAIN 6[5] SELECT[6]		**Tirzepatide** (Mounjaro) SURPASS-CVOT[7]
MACE Hazard Ratio (95% CI)	0.87 (0.78-0.97)	0.91 * (0.83-1.00)	0.88 (0.79-0.99)	0.79 * (0.57-1.11)	0.74 (0.58-0.95)	0.80 (0.72-0.90)	Ongoing
All-cause death Hazard Ratio (95% CI)	0.85 (0.75-0.97)	*	*	0.51 (0.31-0.84)	*	*	

*Not statistically different from placebo group.
CI, confidence interval.

1. Marso SP, et al. *N Engl J Med*. 2016;375(4):311-322.
2. Holman RR, et al. *N Engl J Med*. 2017;377(13):1228-1239.
3. Gerstein HC, et al. *Lancet*. 2019;394(10193):121-130.
4. Husain M, et al. *N Engl J Med*. 2019;381(9):841-851.
5. Marso SP, et al. *N Engl J Med*. 2016;375(19):1834-1844.
6. Lincoff AM, et al. *N Engl J Med* 2023;389(24):2221-2232.
7. Nicholls SJ, et al. *Am Heart J*. 2024;267:1-11.

Cardiovascular Outcomes Trials for GLP-1 RAs

FDA Approval

Major adverse cardiovascular events: MI, stroke, CV death	**Liraglutide** CV risk reduction in T2DM and CVD	**Exenatide ER** (Bydureon) EXSCEL[2]	**Dulaglutide** CV risk reduction in T2DM and CVD or multiple CV	**Oral Semaglutide** (Victoza) PIONEER 6[4]	**SC Semaglutide** CV risk reduction in T2DM and CVD		**Tirzepatide** (Mounjaro) SURPASS-CVOT[7]
MACE Hazard Ratio (95% CI)	0.87 (0.78-0.97)	0.91 * (0.83-1.00)	0.88 (0.79-0.99)	0.79 * (0.57-1.11)	0.74 (0.58-0.95)	0.80 (0.72-0.90)	Ongoing
All-cause death Hazard Ratio (95% CI)	0.85 (0.75-0.97)	*	*	0.51 (0.31-0.84)	*	*	

*Not statistically different from placebo group.
CI, confidence interval.

1. Marso SP, et al. *N Engl J Med*. 2016;375(4):311-322.
2. Holman RR, et al. *N Engl J Med*. 2017;377(13):1228-1239.
3. Gerstein HC, et al. *Lancet*. 2019;394(10193):121-130.
4. Husain M, et al. *N Engl J Med*. 2019;381(9):841-851.
5. Marso SP, et al. *N Engl J Med*. 2016;375(19):1834-1844.
6. Lincoff AM, et al. *N Engl J Med* 2023;389(24):2221-2232.
7. Nicholls SJ, et al. *Am Heart J*. 2024;267:1-11.

FDA Indications for Available GLP-1 RAs and a GLP-1 RA/GIP

GLP-1 RA	Brand Name	T2DM	Primary CVD Prevention	Secondary CVD Prevention	Weight Management
Liraglutide	Victoza	X		X	
	Saxenda				X
Exenatide	Byetta	X			
	Bydureon	X			
Dulaglutide	Trulicity	X	X	X	
Semaglutide	Rebelsus	X			
	Ozempic	X		X	
	Wegovy			X	X
GLP-1 RA/GIP					
Tirzepatide	Mounjaro	X			
	Zepbound				X

From prescribing information from each manufacturer's website, accessed individually on 8/17/24.

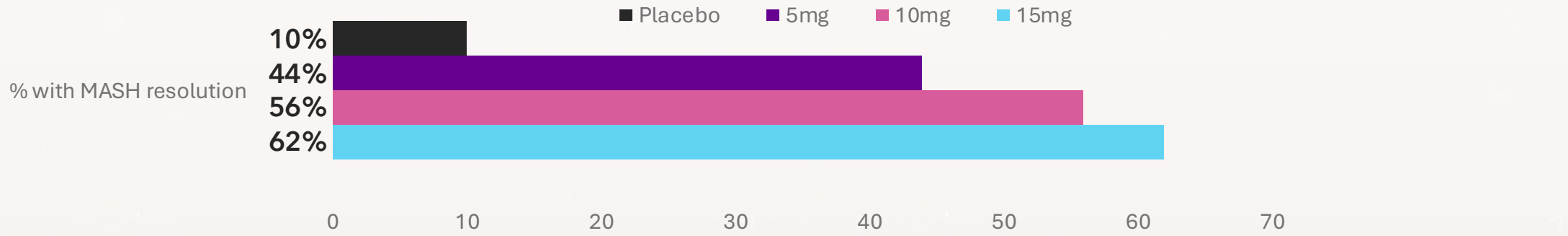
Chronic Kidney Disease Outcomes With GLP-1 RAs

	Liraglutide (Victoza) LEADER[1]	**Dulaglutide** (Trulicity) REWIND[2]	**SC Semaglutide (Ozempic/Wegovy)** SUSTAIN 6[3]	FLOW[4]
Hazard Ratio (95% CI)	0.78 (0.67-0.92)	0.88 (0.79-0.99)	0.64 (0.46 to 0.88)	0.76 (0.66 to 0.88)
CKD endpoint studied	Composite of new-onset persistent macroalbuminuria, persistent doubling of the serum creatinine level, end-stage kidney disease, or death due to kidney disease	Development of urinary albumin-to-creatinine ratio >33.9 mg/mmol, sustained ≥30% decline in estimated glomerular filtration rate (eGFR), or chronic kidney replacement therapy	Composite of persistent macroalbuminuria, persistent doubling of the serum creatinine level, and a creatinine clearance ≤ 45mL/min	Composite of the onset of kidney failure (dialysis, transplantation, or an eGFR of <15 mL/min/1.73 m^2), at least a 50% reduction in the eGFR from baseline, or death from kidney-related or cardiovascular causes

1. Mann JFE, et al. *N Engl J Med*. 2017;377(9):839-848. 2. Gerstein HC, et al. *Lancet*. 2019;394(10193):121-130. 3. Marso SP, et al. *N Engl J Med*. 2016;375(19):1834-1844. 4. Perkovic V, et al. *N Engl J Med*. 2024;391(2):109-121.

Liver Disease and Tirzepatide

- Phase 2 trial in 190 participants with MASH (metabolic dysfunction-associated steatohepatitis) and moderate or severe cirrhosis:
  - Randomized to weekly tirzepatide (5 mg, 10 mg, or 15 mg) or placebo for 1 yr
  - Primary endpoint was resolution of MASH without worsening of fibrosis
  - Key secondary endpoint was improvement of at least 1 fibrosis stage
    - Results for primary endpoint:



Loomba R, et al. *N Engl J Med.* 2024;391(4):299-310.

Multiple Trials Confirm Similar Findings

- Systematic review and meta-analysis of 8 randomized controlled trials of GLP-1 RAs comprising 60,080 patients
  - Reduced:
    - MACE by 14% (95% CI 0.8-0.93) *P* = 0.0001
    - Hospital admission for heart failure by 11%
    - Composite kidney outcome by 21%
    - All-cause mortality by 12%
  - No increase in risk of severe hypoglycemia, retinopathy, or pancreatic adverse effects

MACE, major adverse cardiovascular events (MI, stroke, CV death).
Sattar N, et al. *Lancet Diabetes Endocrinol*. 2021;9(10):653-662.

Learning Objectives

2

Select GLP-1 RAs based on the updated ADA guidelines for T2DM medication management, integrating patient comorbidities and considerations

Selecting a GLP-1 RA for Your Patient

ASCVD

Weight Loss

Pretreatment Cautions

Patient Considerations

Selecting a GLP-1 RA for Your Patient

ASCVD

Choose meds with proven ASCVD risk reduction data:
Liraglutide
Dulaglutide
Semaglutide

Weight Loss

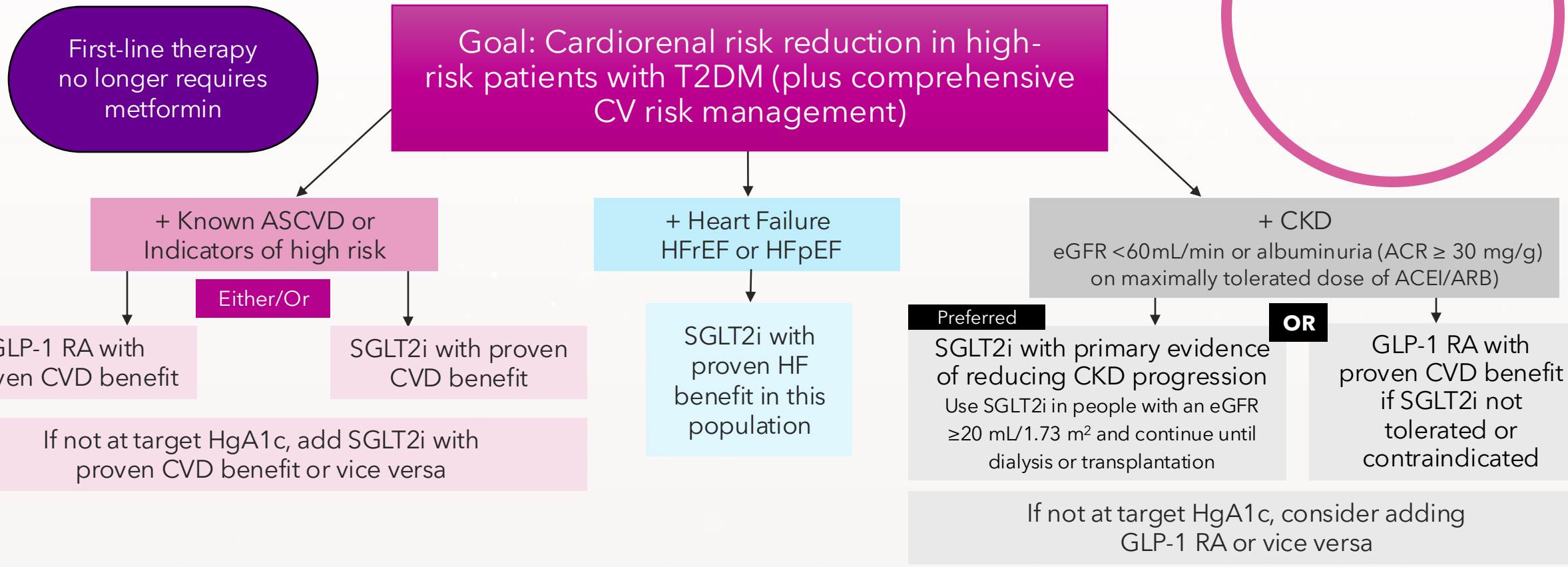
Choose meds with high or very high efficacy for weight loss

2024 ADA Standards of Care: Use of Glucose-Lowering Medications in T2DM

Goal: Cardiorenal risk reduction in high-risk patients with T2DM (plus comprehensive CV risk management)

Goal: Achievement and maintenance of glycemic and weight management goals

2024 ADA Standards of Care: Use of Glucose-Lowering Medications in T2DM



ACEI, angiotensin-converting enzyme inhibitor; ACR, albumin-to-creatinine ratio; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; SGLT2i, sodium-glucose cotransporter 2 inhibitor.

American Diabetes Association Professional Practice Committee. *Diabetes Care*. 2024;47(Suppl 1):S158-S178.

2024 ADA Standards of Care: Use of Glucose-Lowering Medications in T2DM

Goal: Achievement and maintenance of glycemic and weight management goals

Glycemic management: choose approaches that provide the efficacy to achieve goals

- Metformin OR agent(s) including COMBINATION therapy that provide adequate EFFICACY to achieve and maintain treatment goals
- Consider avoidance of hypoglycemia a priority in high-risk individuals

Achievement and maintenance of weight management

Set individualized weight management goals:

- General lifestyle advice: nutrition/eating patterns/physical activity
- Consider weight-loss medication
- Intensive evidence-based weight management program
- Consider metabolic surgery

Efficacy for glucose lowering

Very high: Dulaglutide (high dose), semaglutide, tirzepatide Insulin, combination oral, combination injectable GLP-1 RA/insulin
High: GLP-1 RA (not listed above), SGLT2i, metformin, TZD, sulfonylurea
Intermediate: DPP-4i

Efficacy for weight loss

Very high: Semaglutide, tirzepatide
High: Dulaglutide, liraglutide
Intermediate: GLP-1 RA (not listed above), SGLT2i
Neutral: DPP-4i, metformin

DPP-4i, dipeptidyl peptidase 4 inhibitor; SGLT2i, sodium-glucose cotransporter 2 inhibitor; TZD, thiazolidinedione.

American Diabetes Association Professional Practice Committee. *Diabetes Care*. 2024;47(Suppl 1):S158-S178.

Selecting a GLP-1 RA for Your Patient

ASCVD

Weight Loss

Pretreatment Cautions

Selecting a GLP-1 RA for Your Patient

Pretreatment Cautions

Medullary thyroid cancer and MEN2A/2B

Rodent studies only

No association has been established in humans

Not recommended if patient has family or personal history of either of these

Retinopathy[1]

SUSTAIN 6 only: Increase in retinal complications (hemorrhage, blindness, or conditions requiring laser treatment)
*Thought to be due to rapid glucose-lowering effect of semaglutide

Pancreatitis

Insufficient data to establish causal relationship but not recommended with history of pancreatitis

Renal Impairment

Renal dosing (exenatide)

Gastroparesis

Short-acting agents should not be used in history of gastroparesis

1. Marso SP, et al. *N Engl J Med*. 2016;375(19):1834-1844.

Selecting a GLP-1 RA for Your Patient

ASCVD

Weight Loss

Pretreatment Cautions

Patient Considerations

Selecting a GLP-1 RA for Your Patient

Patient Considerations

Formulation:
- Long or short acting
- Oral vs injectable
- Dexterity for device

Pregnancy Considerations

Office and Insurance Issues

Learning Objectives

3

Individualize treatment plans using the GLP-1 RAs with attention to common patient questions and concerns, including drug shortages

Once You've Started a GLP-1 RA

1. Medication education
   - Manufacturer websites
   - MA/nurse educator
2. Anticipatory guidance, especially side effects
3. Diet and exercise counseling

Office Efficiency Tips

- Use your EMR to your advantage
- Create a consistent phrase for your GLP-1 RA initial visits and follow-up visits to ensure efficient and consistent education
- Clearly document your diagnoses, importance, and medical necessity for the GLP-1 RA along with recent labs and data to expedite access
- Designate a staff member to assist with prior authorizations

Stopping GLP-1 RAs: SURMOUNT-4

- Does once-weekly subcutaneous tirzepatide with diet and physical activity affect maintenance of body weight reduction in individuals with obesity or overweight?
- Multicenter, with open-label lead-in period and then double-blind placebo-controlled trial
- **Open-label lead-in period**: 783 adults with overweight or obesity without diabetes enrolled and received once-weekly subcutaneous tirzepatide (10 or 15 mg) for 36 weeks
- **Intervention**: At week 36, 670 participants (who completed 36 weeks) were randomized (1:1) to continue receiving tirzepatide (n = 335) or switch to placebo (n = 335) for 52 additional weeks
- **Primary Outcome**: Mean percent weight change from randomization at week 36 to week 88
- **Results**:

Tirzepatide	Placebo	
-5.5%	+14.0%	Difference, −19.4% [95% CI, −21.2% to −17.7%]; $P < 0.001$

Aronne LJ, et al. *JAMA*. 2024;331(1):38-48.

Managing GI Side Effects

Anticipatory Guidance

- Remind patients that these drugs work in the brain to reduce appetite, not speed up metabolism
- When feeling full, STOP eating
- Focus on smaller, lower-fat meals
- Encourage hydration: increase water, decrease sugary drinks
- Try crackers, mint, ginger for nausea
- Exercise: resistance bands, weight training

Clinician Recommendations

- In clinical trials only 4%-8% of patients using GLP-1 RAs withdrew consent due to adverse effects
- Use recommended starting doses and titrate slowly; most patients can tolerate well after 4 weeks
- Slow down dose escalations if significant GI issues
- Short-term pharmacologic support:
  - Antiemetics (ondansetron)
  - Probiotics, antidiarrheals, stool softeners as needed
- Consider metformin dose reduction
- Remember to work up extreme cases

Gorgojo-Martínez JJ, et al. *J Clin Med*. 2022;12(1):145.

Missed Doses

- Medication shortages may lead to inadvertent missed doses
- Tolerance to GI side effects is anticipated over time but may vary with inconsistent use
- Individual manufacturers have specific guidance for missed doses…
- Generally:
  - Daily meds: resume at next scheduled dose
  - Weekly injectables: resume as soon as possible, within 3-5 days of missed dose, or skip dose and administer the next dose

Resuming after prolonged lapse:

Agent	Last Dose Administered	Recommendation(s) for Resuming Therapy
Dulaglutide*	1.5 mg once weekly	• Resume at 1.5 mg once-weekly dose. • Expect comparable tolerability to that experienced prior to dose interruption.
	3 or 4.5 mg once weekly	• Use best judgment if ≥3 doses are missed. • It is unknown whether tolerance to the GI adverse events will remain if reinitiated at the higher dose after ≥3 missed doses. • Decision can be informed by patient's prior GI tolerability. • In consideration of the above, clinicians may consider reinitiating at 1.5 mg once weekly.
Injectable semaglutide†	1 mg once weekly	• If ≤2 doses are missed, reinitiate at 1 mg once weekly. • If 3–4 doses are missed, reinitiate at 0.5 mg weekly. • If ≥5 doses are missed, reinitiate at 0.25 mg once weekly.
Tirzepatide‡	≥5 mg once weekly	• If ≤2 doses are missed, reinitiate at the same dose (provided the dose was adequately tolerated). • If ≥3 doses are missed, reinitiate at 5 mg once weekly.

Whitley HP, et al. *Clin Diabetes*. 2023;41(3):467-473.

Alternative Dosing Strategies

Extended-interval dosing:

- Extend the time between injections with intention of supply rationing
  - No clear evidence of this strategy
  - Would not recommend in T2DM management

Multiple smaller doses:

- Dulaglutide and tirzepatide available only as single-dose, single-use pens
  - Ex: could prescribe dulaglutide 1.5 mg twice a week or 2 doses weekly to equal 3 mg dose

Alternate intermediate doses:

- Injectable semaglutide as Ozempic is available as an adjustable multidose pen
  - Allows administration of an alternate/lower dose from higher-dose pen based on number of "clicks" dialed
  - Note shelf life of pen: 56 days

Whitley HP, et al. *Clin Diabetes*. 2023;41(3):467-473.
Ozempic. Prescribing information. Novo Nordisk, Inc; 2023.

Suggested Comparative Doses of GLP-1 RAs for Treating T2DM

Exenatide SC BID	5 mcg	10 mcg					
Liraglutide SC weekly	0.6 mg	1.2 mg	1.8 mg				
ExenatideXR SC weekly			2 mg				
Dulaglutide SC weekly		0.75 mg	1.5 mg	3.0 mg	4.5 mg		
Semaglutide PO daily	3 mg	7 mg	14 mg				
Semaglutide SC weekly		0.25 mg	0.5 mg		1 mg	2 mg	
Tirzepatide SC weekly			2.5 mg			5 mg	≥10 mg no comparisons

Adapted from Whitley HP, et al. *Clin Diabetes*. 2023;41(3):467-473.

Compounded GLP-1 RAs

- FDA allows pharmacies to produce a compounded version of a medication when it is considered in shortage—not "generics," not FDA-approved
  - Injectable semaglutide and tirzepatide are both in shortage, not oral semaglutide[1]
- Compounding pharmacies must meet certain requirements, including[2,3]:
  - Use the same form of medication base in the FDA-approved medications
  - Purchase that base from FDA-registered facilities
  - Compound medication in accordance with state and federal regulations
  - Dispense the compounded medication with a prescription from a licensed healthcare professional

1. https://dps.fda.gov/drugshortages
2. https://www.fda.gov/drugs/human-drug-compounding/compounding-and-fda-questions-and-answers
3. https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/medications-containing-semaglutide-marketed-type-2-diabetes-or-weight-loss

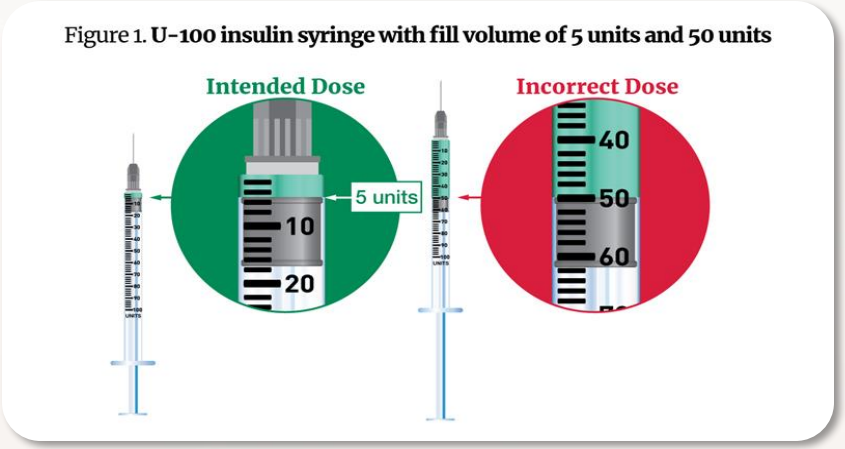
Compounded Semaglutide Errors

FDA reported variances[1]:

- Packaging: could come packaged in multidose vials
- Instructions: units rather than mg or mL
- Salt forms instead of approved base form
- Additional ingredients
  - Vitamin B-12, vitamin B-6, levocarnitine (L-Carnitine), and nicotinamide adenine dinucleotide (NAD)

Case Series[2]:

- 3 patients incorrectly administered semaglutide for weight loss obtained from compounding pharmacies and a spa
  - 10-fold dosing error



1. https://www.fda.gov/drugs/human-drug-compounding/fda-alerts-health-care-providers-compounders-and-patients-dosing-errors-associated-compounded
2. Lambson JE, et al. *J Am Pharm Assoc (2003)*. 2023;63(5):1643-1645.

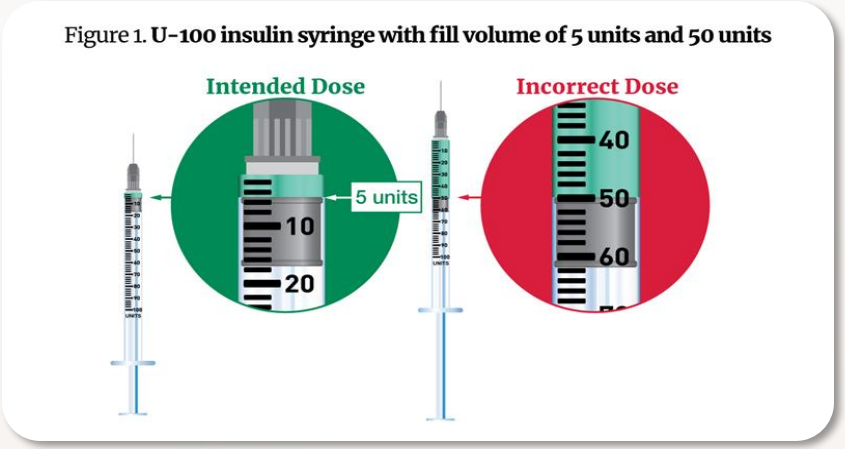
Compounded Semaglutide Errors

FDA reported variances[1]:

- Packaging: could come packaged in multidose vials
- Instructions: units rather than mg or mL
- Salt forms instead of approved base form
- Additional ingredients
  - Vitamin B-12, vitamin B-6, levocarnitine (L-Carnitine), and nicotinamide adenine dinucleotide (NAD)

Case Series[2]:

- 3 patients incorrectly administered semaglutide for weight loss obtained from compounding pharmacies and a spa
  - 10-fold dosing error



1. https://www.fda.gov/drugs/human-drug-compounding/fda-alerts-health-care-providers-compounders-and-patients-dosing-errors-associated-compounded
2. Lambson JE, et al. *J Am Pharm Assoc (2003)*. 2023;63(5):1643-1645.

Compounded GLP-1 RA Guidance

Reputable Online Pharmacies:

- Always require a prescription from a licensed provider
- Provide a physical US address and phone number
- Have a licensed pharmacist on staff to answer your questions
- Licensed with a state board of pharmacy

Key Takeaways

GLP-1 RAs stimulate glucose-dependent insulin release from the pancreas which slows gastric emptying and inhibits post-meal glucagon release, resulting in **decreased appetite and food intake**

GLP-1 RAs and GLP-1 RA/GIP medications are powerful medications in our arsenal to treat T2DM, obesity, heart disease, and more

Choose GLP-1 RA medications based on patient goals, medication efficacy, and individual comorbidities and preferences

Achieve greatest success by discussing coverage issues up front, managing side effects proactively, and educating on the importance of adherence for greatest benefit