GLP-1 RAs UNLOCKED

Transforming T2D Care from Pathology to Practice

Are you familiar with the current and emerging GLP-1 receptor agonist (RA) therapies and their multifaceted benefits?

CASE CHALLENGE

A 45-year-old man with a history of type 2 diabetes (T2D), hypertension, obesity, and established coronary artery disease presents to his rural primary care clinic for post-hospital follow-up. He was recently discharged from a tertiary care center following hospitalization for an acute coronary event, during which he underwent percutaneous coronary intervention with stent placement to his left anterior descending artery.

He is now back in his rural community and presenting for transition of care and optimization of his chronic disease management. His discharge medications include atorvastatin 80 mg daily, aspirin 81 mg daily, clopidogrel 75 mg daily, metformin 1000 mg BID, lisinopril 20 mg daily, and metoprolol succinate 50 mg daily.

Recent labs and findings:

- HbA1c: 8.2%
- eGFR: 62 mL/min/1.73 m^2
- BMI: 34 kg/m^2
- Blood pressure: 142/88 mmHg
- LDL-C: 58 mg/dL
- Urine albumin-creatinine ratio (uACR): 120 mg/g

BID = twice daily; eGFR = estimated glomerular filtration rate; BMI = body mass index; LDL-C = low-density lipoprotein cholesterol.

What systemic effects of GLP-1 RAs would help this patient? How would you decide which GLP-1 RA to prescribe? How would you dose it?

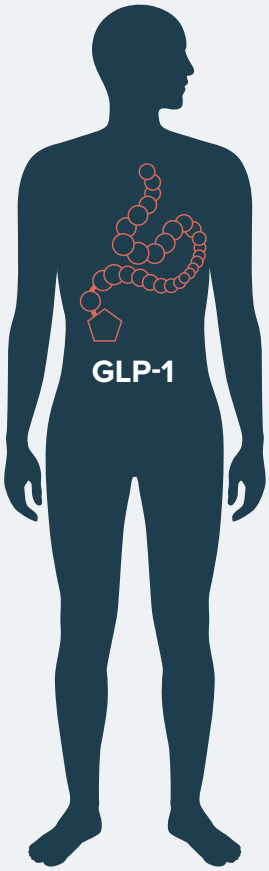
Summary of Key Physiologic Actions of GLP-1

BRAIN
- Neuroinflammation ↓
- Satiety ↑
- Food cravings ↓
- Appetite ↓

HEART
- Cardioprotection ↑
- Cardiac output ↑
- Oxidative stress ↓
- Myocardial glucose uptake ↑
- Atherosclerosis ↓
- Inflammation ↓

LIVER*
- Glucose production ↓
- Steatosis ↓
- Inflammation ↓
- Fibrosis progression ↓

MUSCLE*
- Insulin sensitivity ↑
- Glucose uptake ↑



STOMACH
- ↓ Gastric motility
- ↓ Glycemic spikes
- ↓ Acid production

PANCREAS
- ↑ Insulin sensitivity
- ↑ Glucose uptake
- ↑ β-cell proliferation
- ↓ β-cell apoptosis

GASTROINTESTINAL TRACT
- ↓ Motility in small intestine
- ↓ Inflammation

KIDNEYS
- ↑ Natriuresis
- ↓ Albuminuria
- ↔ Renal perfusion
- ↓ Intraglomerular pressure
- ↓ Glomerular hyperfiltration

GI = gastrointestinal; *GLP-1 actions on liver and muscle are indirect. Drucker DJ. *Cell Metab*. 2006;3:153-165.

Have questions on this topic? Ask the experts!

Scan or click the QR code to submit a question for a chance to have it answered during a live webinar.

FDA-Approved GLP-1 RA and GLP-1 RA/GIP Therapies

Generic Name	FDA-Approved Indications	Starting Dose	Titration Schedule Up-titration should be based on patient tolerance and clinical goals. Maximum doses listed are not target doses, unless specified.
Dulaglutide SC weekly	T2D in patients ≥ 10 years of age MACE reduction in adults with T2D with CVD or multiple CVD risk factors	0.75 mg weekly x 4 weeks	1.5 mg weekly x 4 weeks (dose studied in CVD) 3 mg weekly x 4 weeks 4.5 mg weekly (maximum dosage) **Maintenance doses:** 1.5 mg – 4 mg
Exenatide SC BID	T2D in adults	5 mcg BID x 4 weeks Take doses within 1 hour before a meal (at least 6 hours apart)	10 mcg twice daily (recommended dose, maximum dose)
Exenatide SC weekly		2 mg weekly	N/A
Liraglutide SC daily	T2D in patients ≥ 10 years of age MACE reduction in patients with T2D and established CVD	0.6 mg daily, week 1	1.2 mg daily, week 2 1.8 mg daily (maximum dose, dose studied in CVD) **Maintenance doses:** 1.2 mg or 1.8 mg based on tolerance and glycemic control
	Weight reduction and maintenance in patients ≥ 12 years of age with body weight > 60 kg and obesity Adults with overweight in the presence of at least one weight-related comorbidity	0.6 mg daily, week 1 Any time of day without regard for meals	1.2 mg daily, week 2 1.8 mg daily, week 3 2.4 mg daily, week 4 3.0 mg (target dose, lower doses are for titration only)
Semaglutide SC weekly	T2D MACE reduction in patients with T2D and established CVD Reduce risk of eGFR decline, ESRD, and CV-related death in adults with T2D and CKD	0.25 mg x 1 week 1	0.5 mg x 1 week 2 1 mg x 1 week 3 2 mg x 1 weekly (maximum dose) **Maintenance doses:** T2D, MACE risk reduction: 0.5 mg, 1 mg, or 2 mg, based on tolerance and glycemic control (0.5 mg and 1 mg were studied in CVD) CKD: 1 mg weekly
	Weight reduction and maintenance in patients ≥ 12 years of age with obesity Adults with overweight in the presence of at least one weight-related comorbidity MACE reduction in patients with established CVD and either obesity or overweight	0.25 mg weekly × 4 weeks	0.5 x 4 weeks 1 mg x 4 weeks 1.7 mg x 4 weeks 2.4 mg (maximum dose) **Maintenance doses:** 2.4 mg (recommended) or 1.7 mg based on tolerance (2.4 mg was studied in CVD)

Generic Name	FDA-Approved Indications	Starting Dose	Titration Schedule Up-titration should be based on patient tolerance and clinical goals. Maximum doses listed are not target doses, unless specified.
Semaglutide Oral daily	T2D	3 mg daily × 30 days	7 mg x 30 days 14 mg (maximum dose) **Maintenance doses** 7 mg or 14 mg based on tolerance and glycemic control
Tirzepatide SC weekly	T2D	2.5 mg weekly × 4 weeks	5 mg weekly x 4 weeks 7.5 mg weekly x 4 weeks 10 mg weekly x 4 weeks 12.5 mg weekly x 4 weeks 15 mg weekly (maximum dose) **Maintenance doses** T2D: 5 mg-15 mg based on tolerance and glycemic control Obesity: 5 mg-15 mg based on tolerance OSA: 10 mg and 15 mg doses
	Adults with obesity in the presence of at least one weight-related comorbidity OSA in adults with obesity	2.5 mg weekly × 4 weeks	

CVD = cardiovascular disease; CKD = chronic kidney disease; MACE = major adverse cardiovascular events; ESRD = end-stage renal disease; OSA = obstructive sleep apnea, SC = subcutaneous; CKM = cardiovascular-kidney-metabolic.

WHY THIS MATTERS

- Knowing when a GLP-1 RA should be considered in patients with significant multimorbidity can improve outcomes
- Knowing how to select the correct dose and titration schedule can help decrease side effects and increase adherence
- This program will aid clinicians by providing foundational education on the systemic effects of GLP-1 RAs as well as how to effectively assess if they will benefit complex patients

> *Watch CME Outfitters' 6-episode webcast series on CKM health and GLP-1 RAs to learn more! Complete all 6 activities and claim your badge as a Patient-First Diabetes Management Champion!*

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