



School of Continuous
Professional
Development

OVERCOMING THE AGONIES OF GLP-1 AGONISTS

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DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIP(S) WITH INELIGIBLE COMPANIES

- Nothing to disclose

REFERENCES TO OFF-LABEL USAGE(S) OF PHARMACEUTICALS OR INSTRUMENTS

- Semaglutide
- Tirzepatide

All relevant financial relationships have been mitigated.

DEFINITIONS

- BID – Twice Daily
- BMI – Body Mass Index
- CBT – Cognitive Behavioral Therapy
- CDC – Center for Disease Control
- CKD – Chronic Kidney Disease
- CVD – Cardiovascular Disease
- FDA – Food and Drug Administration
- GLP-1– Glucagon-like Peptide-1
- GI – Gastrointestinal
- GIP – Glucose-Dependent Insulinotropic Polypeptide
- HbA1c – Hemoglobin A1c
- HTN – Hypertension
- MEN 2 – Multiple Endocrine Neoplasia Syndrome Type 2
- MI – Myocardial Infarction
- MTC – Medullary Thyroid Cancer
- MTM – Medication Therapy Management
- N/V/D - nausea, vomiting, diarrhea
- PO – By Mouth
- RA – Receptor Agonist
- SC – Subcutaneously
- T2DM – Type II Diabetes Mellitus

LEARNING OBJECTIVES



Review FDA indications for use of GLP-1/GIP RAs



Understand provider pharmacist collaboration surrounding GLP-1/GIP therapy



Describe challenges with cost effective procurement of GLP-1 therapy



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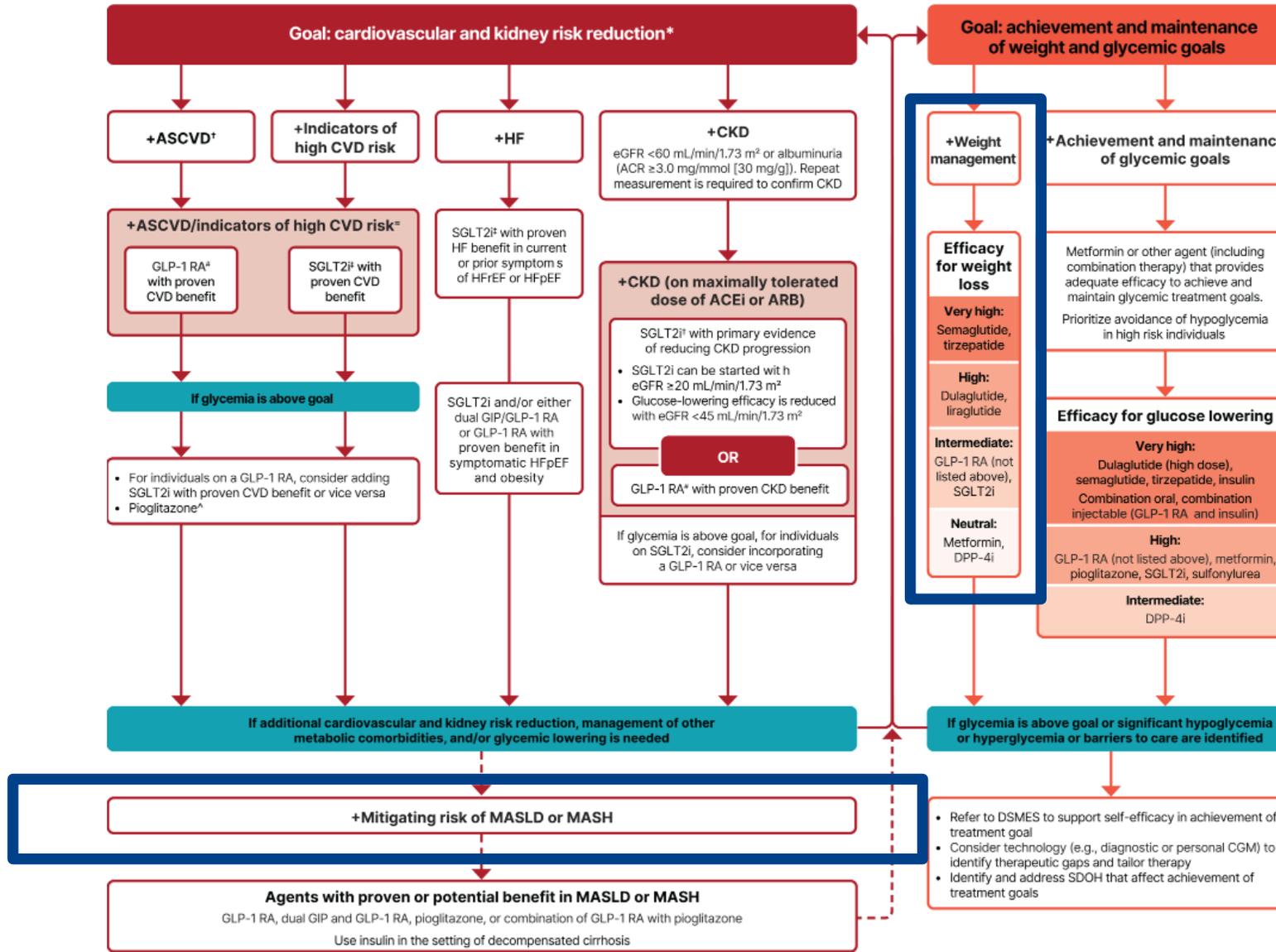
GLP-1/GIP AGONIST USE IN TYPE 2 DIABETES MELLITUS & WEIGHT MANAGEMENT

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)

Healthy lifestyle behaviors; diabetes self-management education and support; social determinants of health

To avoid therapeutic inertia, reassess and modify treatment regularly (3–6 months)



INTERCHANGEABILITY

GLP-1 Receptor Agonists Approved for Treating Type 2 Diabetes											
Agent	Frequency	Equivalent Doses									
Exenatide (Byetta)	SC Twice Weekly	5 mcg	10 mcg								
Lixisenatide (Adlyxin)	SC Daily	10 mcg	20 mcg								
Liraglutide (Victoza)	SC Daily	0.6 mg	1.2 mg	1.8 mg							
Exenatide XR (Bydureon)	SC Weekly			2 mg							
Dulaglutide (Trulicity)	SC Weekly		0.75 mg	1.5 mg	3 mg	4.5 mg					
Semaglutide (Ozempic)	SC Weekly		0.25 mg	0.5 mg		1 mg	2 mg				
Semaglutide (Rybelsus)	PO Daily	3 mg	7 mg	14 mg							
Tirzepatide (Mounjaro)	SC Weekly			2.5 mg			5 mg	7.5 mg	10 mg	12.5 mg	15 mg

INTERCHANGEABILITY

GLP-1 Receptor Agonists Approved for Treating Obesity										
Agent	Frequency	Equivalent Doses								
Semaglutide (Wegovy)	PO Daily	1.5 mg	4 mg	9 mg			25 mg			
Semaglutide (Wegovy)	SC Weekly		0.25 mg	0.5 mg	1 mg	1.7 mg	2.4 mg			
Tirzepatide (Zepbound)	SC Weekly			2.5 mg		5 mg	7.5 mg	10 mg	12.5 mg	15 mg
Liraglutide (Saxenda)	SC Daily	0.6 mg	1.2 mg	1.8 mg	2.4 mg	3mg				

CONTRAINDICATIONS AND ADVERSE EFFECTS

- **Contraindications**

- Personal or family history of MTC
- MEN 2
- Hypersensitivity
- Pregnancy & breastfeeding

- **Precautions**

- History of Pancreatitis

- **Black Box Warning**

- Risk of thyroid C-cell tumors

- **Adverse Effects (AE)**

- N/V/D
- Constipation
- Abdominal pain
- Bloating
- GERD
- Injection-site reaction
- Visual changes
- **Hair loss**

GASTROINTESTINAL GUIDANCE

Anesthesia

- Delayed gastric emptying
- Daily dosing: **hold 1 day prior**
- Weekly dosing: **hold 7 days prior**
- Half life for weekly agents
 - 7 days
 - 4-5 half lives to achieve steady state concentrations

Colonoscopy & Endoscopy

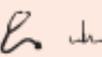
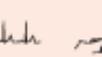
- Increased residual gastric contents
- Inadequate bowel prep colonoscopy
- Incomplete passage through small intestine for capsule endoscopy
- **Hold for 7-21 days**

CLINICAL OBESITY

BMI

WHO CLASSIFICATION OF WEIGHT STATUS	
WEIGHT STATUS	BODY MASS INDEX (BMI), kg/m ²
Underweight	<18.5
Normal range	18.5 – 24.9
Overweight	25.0 – 29.9
Obese	≥ 30
Obese class I	30.0 – 34.9
Obese class II	35.0 – 39.9
Obese class III	≥ 40

Chronic Disease Management

	Preclinical obesity	Clinical obesity
Excess adiposity	✓  + ✓ 	✓  + ✓ 
Mechanisms and pathophysiology	Alterations of cells and tissue → Alterations of organ structure	Alterations of organ function → End-organ damage
Clinical manifestations	Minor or absent (substantially preserved organ function)	Signs and symptoms Limitations of daily activities Complications
Detection and diagnosis	Anthropometrics, medical history, review of organ systems, and further diagnostic assessment as needed	
	  	  

WEGOVY (SEMAGLUTIDE)

- **SUSTAIN Trial**
 - **Design:** RCT, double-blind, multicenter, placebo-controlled
 - **Participants:** with and without PAD
 - **Primary Outcome:**
 - **Composite of CV death, non-fatal MI, or non-fatal stroke (MACE)**
 - **Results:**
 - Patients with PAD: 7% semaglutide vs 11.7% placebo
 - Patients without PAD: 6.5% semaglutide vs 8.4% placebo
 - **Conclusion:** semaglutide **REDUCES MACE** with consistent CV efficacy regardless of PAD status

ZEPBOUND (TIRZEPATIDE)

- **SURMOUNT Tirzepatide vs Placebo**
- **Design:** two phase 3, double-blind, RCT
- **Participants:** adults with **moderate-to-severe** obstructive sleep apnea and obesity
 - Moderate: 15-29 events per hour
 - Severe: ≥ 30 events per hour
- **Primary End Point:** Change in the AHI from baseline
- **Result: Mean Change in AHI at 52 weeks**
 - **Trial 1:** -25.3 events per hour vs -5.3 events per hour
 - **Trial 2:** -29.3 events per hour vs -5.5 events per hour
- **Conclusion:** Tirzepatide reduced the AHI, body weight, hypoxic burden, high-sensitivity C-reactive protein concentration, and SBP and improved sleep-related patient-reported outcomes

MAINTENANCE THERAPY

- Across the four BMI categories of overweight, class I, class II, and class III obesity, the median time to **weight plateau was 6 to 9 months**
- **Longer time to plateau association:**
 - Higher doses of tirzepatide (10 and 15 mg)
 - Younger age
 - Female sex



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PHARMACIST PROVIDER COLLABORATION

IMPACT AT MAYO CLINIC

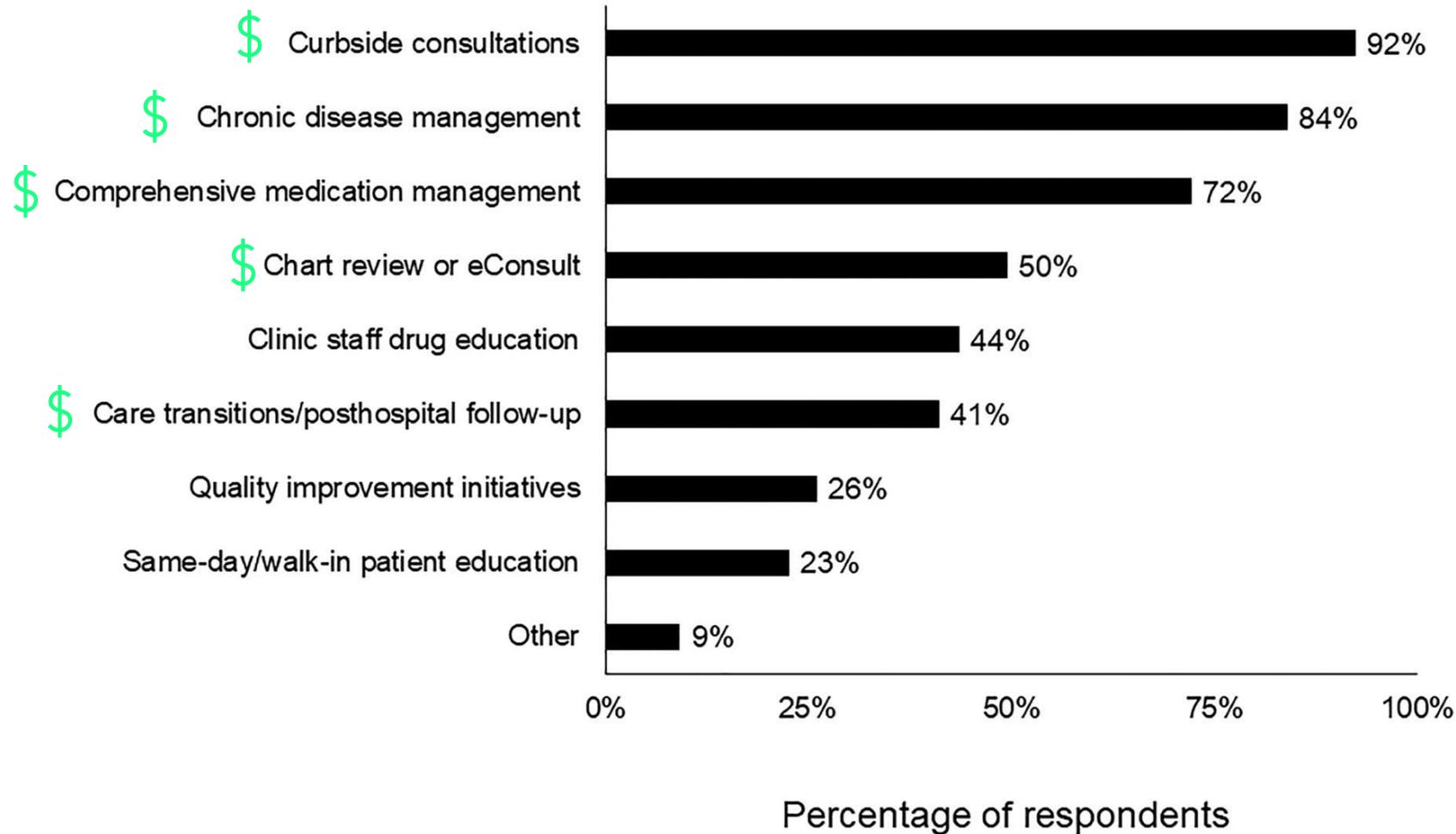
ORIGINAL RESEARCH

Effect of an Integrated Clinical Pharmacist on the Drivers of Provider Burnout in the Primary Care Setting

Jordan D. Haag, PharmD, Kaitlin J. Yost, PharmD, Kimberly A. Kosloski Tarpenning, PharmD, Audrey J. Umbreit, PharmD, Sarah A. McGill, PharmD, Amy L. Rantala, MD, James A. Storlie, MD, Jay D. Mitchell, MD, Ross A. Dierkhising, MS, and Nilay D. Shah, PhD

- 300 providers surveyed
 - 40% response
- ≥ 2 years of collaboration
- 90% agreement that pharmacist collaboration reduced burnout
 - 4 primary drivers
 - Job demands
 - Efficiency and resources
 - Meaning in work
 - Social support and community at work

PROVIDER REASONS FOR PHARMACIST UTILIZATION FOR COLLABORATION ACTIVITIES





THE INSURANCE PROCESS

INSURANCE CONSIDERATION

- **FDA Approval for Type 2 Diabetes Mellitus**

- Ozempic: semaglutide
- Rybelsus: semaglutide oral
- Trulicity: dulaglutide
- Mounjaro: tirzepatide
- Victoza: liraglutide

- **FDA Approval for Weight Loss**

- Wegovy oral and injection: semaglutide
- Zepbound: tirzepatide
- Saxenda: liraglutide

- **FDA Approval for Metabolic Dysfunction-Associated Steatohepatitis (MASH)**

- Wegovy oral and injection: semaglutide

- **FDA Approval for established cardiovascular disease (MI, stroke, PAD)**

- Wegovy oral and injection: semaglutide

Medicare, Commercial, Medicaid
MASH – Wegovy (Screening)
MI – Wegovy
Stroke – Wegovy
OSA – Zepbound (Screening)
PAD – Wegovy (Screening)

INSURANCE COVERAGE



Average Retail Price

\$1200 monthly



Average Compounded Price

\$250 monthly



**Insurance Approval
Requirements**

Baseline weight within 30 days and at 3 month intervals
PA
Appeals

PRIOR AUTHORIZATION

- **Providers spend on average up to 5 hours a week on PAs**
 - 364 hours in a year = ~15.2 days
- Utilization of Artificial Intelligence (AI)

Prompt: "Please write an appeal letter for a 67-year-old male patient with Humana Medicare part D who needs Zepbound AHI 42 BMI 34. Comorbidities include prediabetes, HTN, hyperlipidemia, fatty liver disease, knee osteoarthritis"

Letter

Insurance Appeal Letter for Tirzepatide (Zepbound)

RE: Appeal for Coverage of Tirzepatide (Zepbound) for [Patient Name], DOB: [DOB], Member ID: [ID Number]

Dear Humana Medicare Part D Medical Director,

I am writing to appeal the denial of coverage for tirzepatide (Zepbound) for my patient, a 67-year-old male with obesity (BMI 34 kg/m²) and severe obstructive sleep apnea (AHI 42 events/hour), along with multiple weight-related comorbidities including prediabetes, hypertension, hyperlipidemia, non-alcoholic fatty liver disease, and knee osteoarthritis.

FDA-Approved Indication and Clinical Rationale

Tirzepatide is FDA-approved for chronic weight management in adults with obesity or overweight in the presence of at least one weight-related comorbid condition.^{[1][2]} This patient meets criteria with a BMI of 34 kg/m² and multiple weight-related comorbidities. Most significantly, in December 2024, the FDA approved tirzepatide as the first prescription medication for the treatment of moderate-to-severe obstructive sleep apnea in adults with obesity, making this patient an ideal candidate for this therapy.^[2]

Evidence for Obstructive Sleep Apnea Treatment

This patient's severe obstructive sleep apnea (AHI 42 events/hour) represents a critical indication for tirzepatide therapy. The landmark SURMOUNT-OSA trials published in the New England Journal of Medicine demonstrated that tirzepatide reduced the apnea-hypopnea index by 20.0-23.8 events per hour compared to placebo (p<0.001), representing a 50.7-58.7% reduction from baseline.^[3] In patients with baseline AHI similar to this patient, tirzepatide reduced AHI by approximately 25-29 events per hour at 52 weeks.^[3]

Beyond AHI reduction, tirzepatide significantly improved sleep apnea-specific hypoxic burden by 61.3-70.1% min/hour, reduced systolic blood pressure by 3.7-7.6 mm Hg, and decreased high-sensitivity C-reactive protein by 0.7-1.0 mg/L.^[3] A recent meta-analysis confirmed that incretin-based therapies reduced AHI by a mean of 14.45 events/hour

References

References

1. **Clinical Management of Obesity - Third Edition.** Caroline M. Apovian MD, Louis Aronne MD, Sarah R. Barenbaum MD. The Obesity Society (2025)
2. **American Association of Clinical Endocrinology Consensus Statement: Algorithm for the Evaluation and Treatment of Adults With Obesity/Adiposity-Based Chronic Disease - 2025 Update.** Nadolsky K, Garvey WT, Agarwal M, et al.. Endocrine Practice : Official Journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists. 2025;31(11):1351-1394. doi:10.1016/j.eprac.2025.07.017.
3. **Tirzepatide for the Treatment of Obstructive Sleep Apnea and Obesity.** Malhotra A, Grunstein RR, Fietze I, et al.. The New England Journal of Medicine. 2024;391(13):1193-1205. doi:10.1056/NEJMoa2404881.
4. **Efficacy of Incretin-Based Therapies in Obesity-Related Obstructive Sleep Apnea: A Systematic Review and Meta-Analysis of Randomized Controlled Trials.** Bardóczy A, Matics ZZ, Turan C, et al.. Sleep Medicine Reviews. 2025;82:102119. doi:10.1016/j.smrv.2025.102119.
5. **Incretin Receptor Agonists and CPAP Use in Adults With Diabetes, Obesity, and Obstructive Sleep Apnea.** Huilin Tang, PhD, MS, Bingyu Zhang, MS, Yiwen Lu, BS, et al. JAMA Network Open. 2025. doi: 10.1001/jamanetworkopen.2025.50978.
6. **Obesity Management in Adults: A Review.** Elmaleh-Sachs A, Schwartz JL, Bramante CT, et al.. JAMA. 2023;330(20):2000-2015. doi:10.1001/jama.2023.19897.
7. **Approach to Obesity Treatment in Primary Care: A Review.** Yanovski SZ, Yanovski JA.. JAMA Internal Medicine. 2024;184(7):818-829. doi: 10.1001/jamainternmed.2023.8526.
8. **Tirzepatide Once Weekly for the Treatment of Obesity.** Jastreboff AM, Aronne LJ, Ahmad NN, et al.. The New England Journal of Medicine. 2022;387(3):205-216. doi:10.1056/NEJMoa2206038.

PRIOR AUTHORIZATION

- A patient's biggest advocate needs to be the patient
- Patient involvement

Member

Name: Jane Doe
Medicaid ID: 000000
DOB: XX/XX/XXX
EFFECTIVE DATE: XX/XX

PCP NAME: Janet Doe
PCP PHONE: XXX-XXX-XXXX

Managed Care

Envolve Pharmacy Solutions

Pharmacy Help Desk:
X-XXX-XXXX

RXBIN: 000000
RXPCN: 000000
RXGRP: 000000

This card is for identification purposes only and is not a guarantee of coverage. Printed: 07-19-2024

Medical:	In Network	Out of Network
Ded:	\$500	\$1,000
OOPM:	\$8,500*	\$17,000

*Includes pharmacy

Call GEHA Clinical at 866-494-4502 for plan required prior authorization.
FAILURE TO CALL FOR PRIOR AUTHORIZATION MAY REDUCE BENEFITS

For Members:	GEHA.com	800-821-6136
CVS Caremark@:	info.caremark.com/oe/geha	844-443-4279
Nurse Advice Line:	RN available 24/7	888-257-4342
	Outside the US call collect	709-835-8243

For Providers:	GEHA.com	800-821-6136
Pharmacy Help Desk:		800-364-6331

Claims: EDI# 39026
GEHA, PO Box 21172, Eagan, MN 55121

COMPOUNDING

FDA COMPOUNDED GLP-1/GIP AGONIST STATEMENT

- Might be appropriate if a medical need cannot be met by an FDA-approved drug, or the FDA-approved drug is not commercially available. **Compounded drugs are not FDA approved**
- **Examples:**
 - Cost prohibitiveness
 - Medicare weight loss pharmacotherapy stipulations
 - Obesity
 - Zepbound - OSA
 - Obesity or overweight
 - Wegovy – Stroke, MI, PAD, MASH

FDA RECOMMENDATIONS FOR PATIENTS



Patients should obtain a prescription from **THEIR** clinician



Should be dispensed from a **state licensed** pharmacy



Visit FDA's [BeSafeRx](#) to ensure online pharmacy reputability



Talk to your **clinician & pharmacist** about safety and efficacy

FDA COMPOUNDED GLP-1/GIP AGONIST STATEMENT

- **Dosing Concerns:**
 - Multiple reports related to dosing **ERROR**
 - Patient self-administration errors
 - Milligrams, units, and milliliters on RX labeling
 - Healthcare professionals inaccurate dosing
 - Increased dosing frequency inappropriately
 - Increased dose strength more quickly
 - Symptoms Reported:
 - N/V/D
 - Abdominal pain
 - Constipation

GLP-1/GIP AGONIST COMPOUNDING CONTINUED

- The FDA does not review compounded GLP-1 agonist for safety, effectiveness, and quality before they are marketed
- **Efficacy**
 - Compounded GLP-1 have similar efficacy to manufactured GLP-1 medications. Compounded ADEs are related to GLP-1 common side effects
- **Harm**
 - As of July 31, 2025, FDA has received:
 - more than 605 reports of ADE with compounded semaglutide
 - more than 545 reports of ADE with compounded tirzepatide

GLP-1/GIP AGONIST COMPOUNDING CONTINUED

- **Cost**

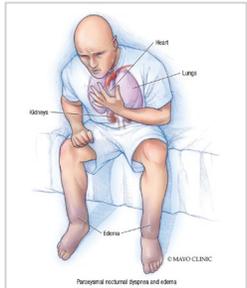
- Non-compounded GLP-1s are **no longer cost prohibitive**
 - Multiple savings programs
 - [Wegovy Savings Card - NovoCare](#)
 - [Mounjaro Savings Card](#)
 - [Zepbound Savings Card](#)
 - [LillyDirect Program](#)



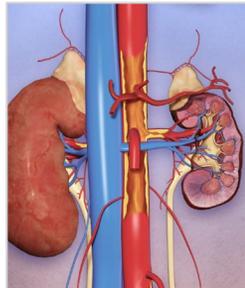
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OFF-LABEL GLP-1/GIP AGONISTS THERAPY

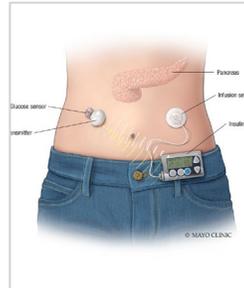
ADJUNCTIVE THERAPY AND FUTURE INDICATIONS



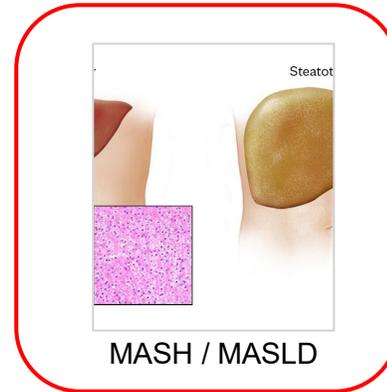
Heart Failure



Chronic Kidney Disease



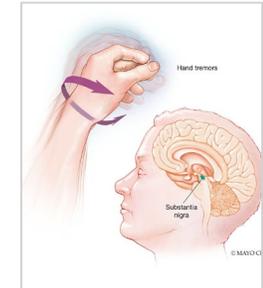
Type 1 DM



Recent FDA approval



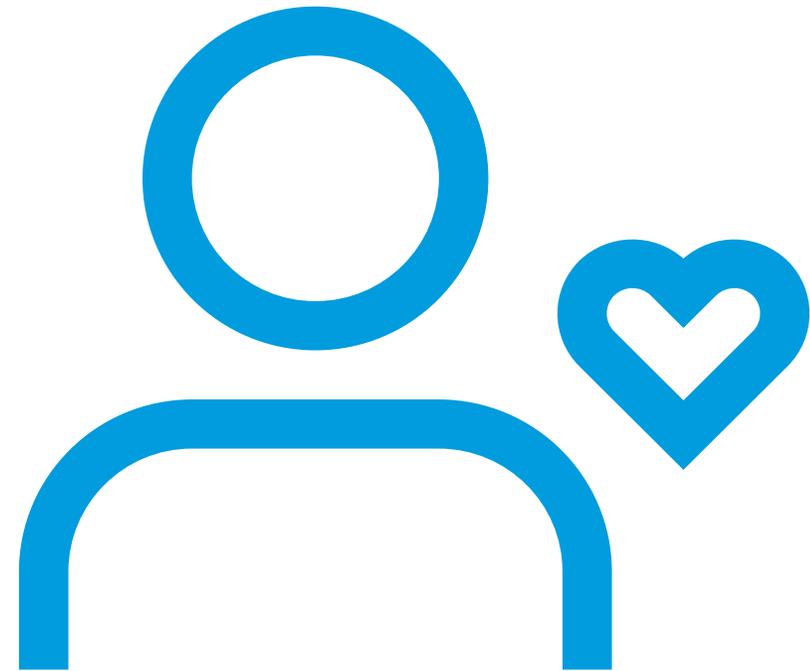
Addiction Medicine



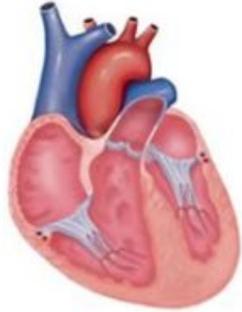
Parkinsons

HEART FAILURE PRESERVED EJECTION FRACTION

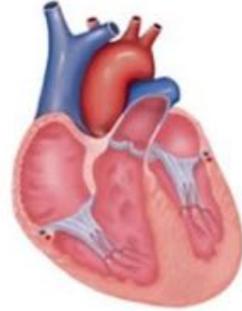
- **GLP-1 RA Benefit:**
 - Reducing ischemic events in patients with HFpEF with a high atherosclerotic risk
- **GLP-1 RA No Benefit:**
 - Reduction in HF-related events in patients with T2DM + HF
- **Recommendation:**
 - SGLT2 inhibitor (first-line agent) + GLP-1 RA (adjunctive) may be used to reduce ASCVD events if the atherosclerotic risk is high



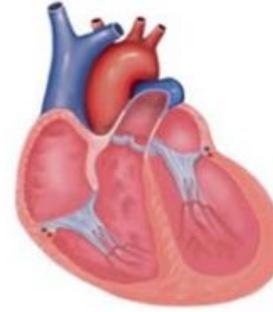
EFFECTS OF GLP1-RA ON HF EVENTS IN PATIENTS WITH TYPE 2 DIABETES



Normal Heart Function



Stable Heart Failure**



Advanced HFrEF***

Risk of HFH or CV Death*



Evidence from RCTs

LEADER, EXSCEL
HARMONY, REWIND, GRADE

LEADER, EXSCEL
HARMONY, REWIND

FIGHT,
LIVE

Proportion of T2D patients



Absolute risk of HF events



- ↓ ASCVD
- ↓ HbA1c
- ↓ BMI
- ↓ BP

Mechanisms of protection

Mechanisms of increased risk

- ↑ cAMP
- ↑ Arrhythmia
- ↑ HR

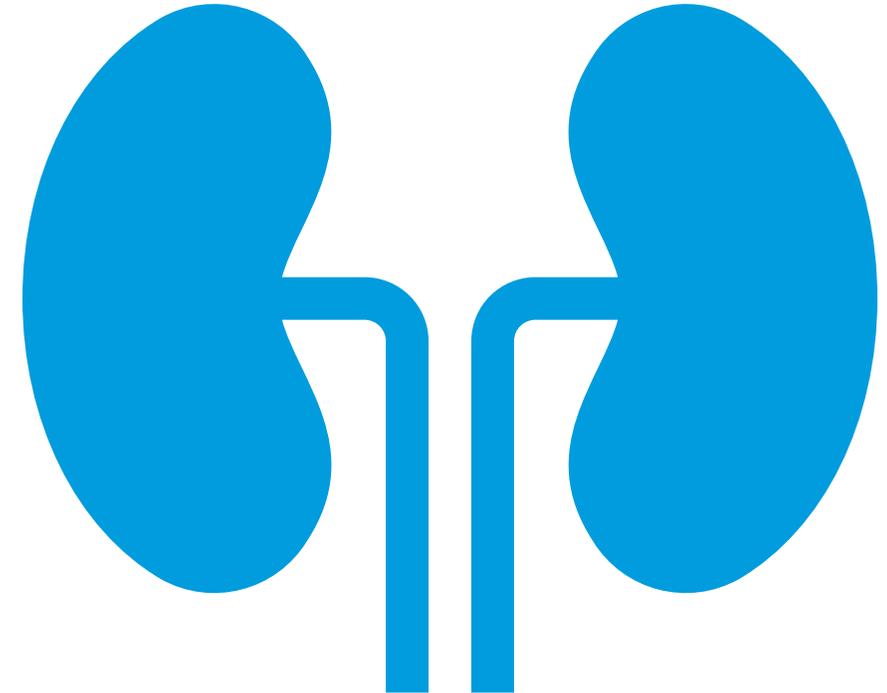
* Reduction of ASCVD events with GLP1-RA is independent of HF status (HR ~0.85)

** Risk of HF events with GLP1-RA may be lower for HFpEF and higher for HFrEF

*** No data available for advanced HFpEF

CKD

- **GLP-1 RA Benefits**
 - Reduce risk for composite kidney disease outcome
 - Macroalbuminuria
 - EGFR decline
 - Progression to kidney failure
 - Death from kidney disease
 - Reduced risk of MACE in patients with T2D
- **KDIGO and ADA Recommends for GLP-1 RA:**
 - Patients with T2DM and CKD who do not meet their individualized glycemic target with metformin and/or an SGLT2i or who are unable to use these drugs



T1DM

- **GLP-1 RA Benefits as adjunct therapy**
 - Weight loss
 - Reduction in A1C
 - Reduce daily insulin dose
 - Improve glycemic control
 - Reduce glucose variability
 - ASCVD risk reduction
- **No risk of developing DKA or severe hypoglycemia**

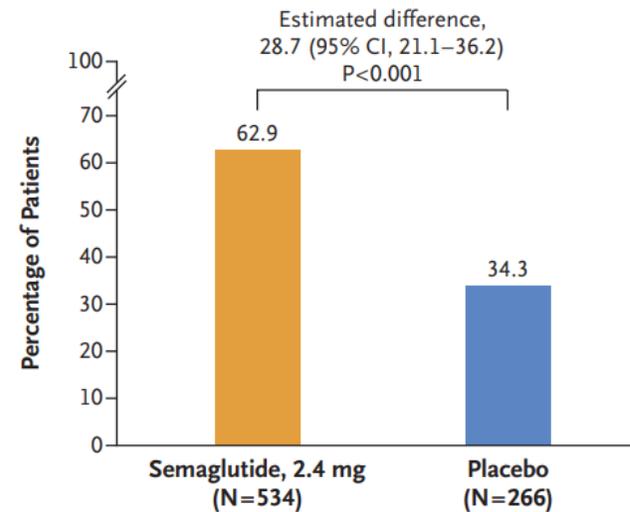


METABOLIC DYSFUNCTION ASSOCIATED STEATOHEPATITIS

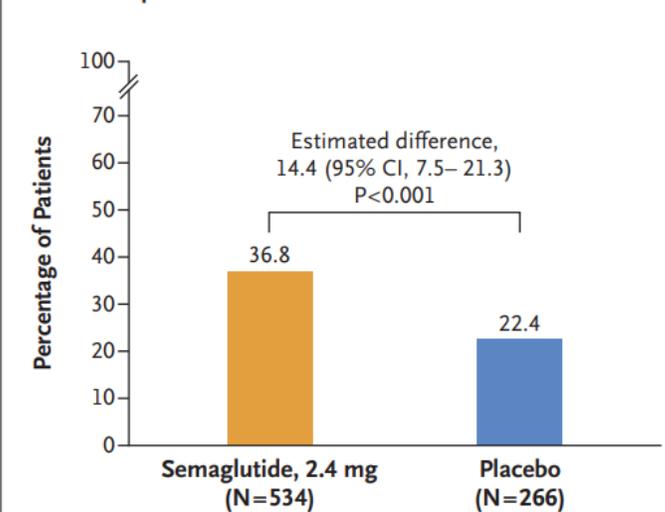
- **Semaglutide Phase 3 Trial**

- Resolution of steatohepatitis without worsening of liver fibrosis
- Reduction in:
 - Liver fibrosis
 - Aminotransferase
 - Liver stiffness
 - ELF score

A Resolution of Steatohepatitis with No Worsening of Liver Fibrosis



B Reduction in Liver Fibrosis with No Worsening of Steatohepatitis



ADDICTION

- Overall preclinical and clinical research has shown GLP-1 agonists to have possible impact on addiction, but the mechanism is not known
- **Categories of addiction GLP-1 therapy may be useful for:**
 - Alcohol
 - Nicotine
 - Stimulants
 - Opioids
 - Cocaine



PARKINSONS DISEASE

- GLP1 agents may be most beneficial within the first 3 years of diagnosis
- Prior studies with **daily** use agents
- Improvements seen in motor function
- Improvements seen in cognitive dysfunction
- **Not recommended as disease modifying at this time**
 - Consider for Parkinson's patients with applicable comorbidities

	Progression of CKD	ASCVD	Heart failure	Glucose-lowering efficacy	Hypoglycemia risk	Weight effects	Cost
Metformin	Neutral	Potential benefit	Potential benefit	High	Low	Neutral	Low
SGLT2 inhibitors	Benefit ^a	Benefit ^c	Benefit	Intermediate	Low	Loss	High
GLP-1 receptor agonists	Benefit ^b	Benefit ^c	Potential benefit	High	Low	Loss	High
DPP-4 inhibitors	Neutral	Neutral	Potential risk ^c (saxagliptin)	Intermediate	Low	Neutral	High
Insulin	Neutral	Neutral	Neutral	Highest	High	Gain	High (analogues)
							Low (human)
Sulfonylureas	Neutral	Neutral	Neutral	High	High	Gain	Low
Thiazolidinediones	Neutral	Potential benefit (pioglitazone)	Increased risk	High	Low	Gain	Low
α-Glucosidase inhibitors	Neutral	Neutral	Neutral	Intermediate	Low	Neutral	Low

Neutral

Potential benefit or intermediate glucose-lowering efficacy

Benefit (organ protection, high efficacy, low hypoglycemia risk, weight loss, or low cost)

Potential risk or high cost to patient

Increased risk for adverse effects

SUMMARY

- **Medical conditions that benefit from GLP-1/GIP RAs:**

- T1DM and T2DM
- Overweight and Obesity
- OSA
- CKD
- HFpEF
- ASCVD
- MASH / MASLD

- **Medical conditions that may benefit from GLP-1/GIP RAs:**

- Addiction

- **Medical conditions to have precaution with GLP-1/GIP RA:**

- HFrEF
- Chronic Pancreatitis

- **Medical conditions that should **AVOID** GLP-1/GIP RA:**

- Pregnancy
- MTC & MEN2



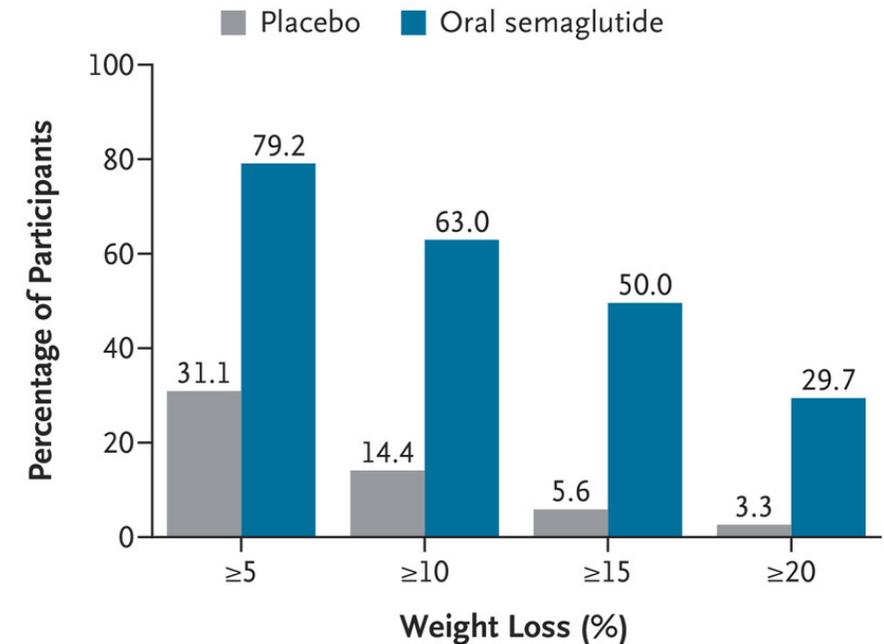
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RESEARCH AND DEVELOPMENT

Oral Semaglutide

- **OASIS 4-** Oral Semaglutide at a Dose of 25 mg in Adults with Overweight or Obesity
- Adverse event: Gastrointestinal adverse events were reported in 151 (74.0%) participants with oral semaglutide 25 mg and 43 (42.2%) with placebo.
- Phase 3 result: In adults with overweight or obesity, oral semaglutide 25 mg once per day led to a significant decrease in bodyweight compared with placebo

B Participants Meeting Weight-Loss Targets at Week 64



TAKE HOME POINTS

1

New FDA Indication

MASH

2

PA Process

Utilize your resources
Patient involvement

3

Oral GLP1s

Similar efficacy
Alternative treatment route
Better price

QUESTIONS & ANSWERS

