MAKING SENSE OF GLP1 AND GIPS IN CLINICAL PRACTICE

Belinda “Lindy” P. Childs, APRN-CNS, BC-ADM, CDCES

1

MAKING SENSE OF GLP1 AND GIPS
IN CLINICAL PRACTICE

Disclosures: No disclosures in past 48 months

2

OBJECTIVES

- Identify risk and benefits of GLP1/GIP class of diabetes medications
- Provide clinical pearls for use of GLP1/GIP class of medications

3

CLASSIFICATION.

Diabetes can be classified into the following general categories:

1. Type 1 diabetes (due to autoimmune ß-cell destruction, usually leading to absolute insulin deficiency)
2. Type 2 diabetes (due to a progressive loss of ß-cell insulin secretion frequently on the background of insulin resistance)
3. Gestational diabetes mellitus (GDM) (diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation)
4. Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young [MODY]), diseases of the exocrine pancreas (such as cystic fibrosis and pancreatitis), and drug- or chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation)

Classification and Diagnosis of Diabetes:
Standards of Medical Care in Diabetes - 2019. Diabetes Care 2019;42(Suppl. 1):S13-S28

4

4

Staging of Type 1 Diabetes

Table 2.1—Staging of type 1 diabetes (4,5)

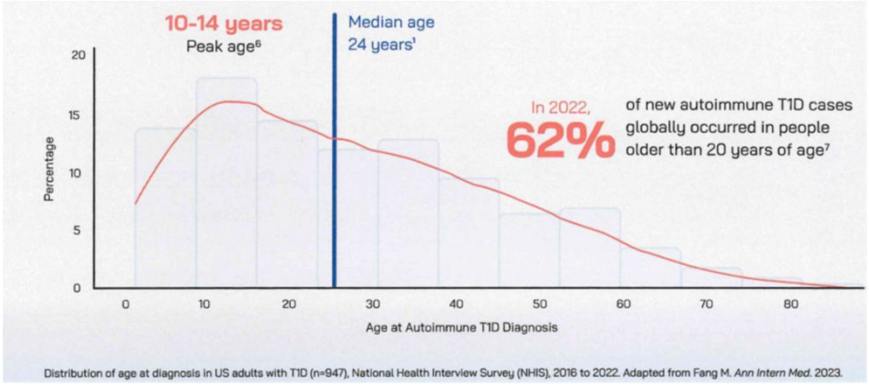
	Stage 1	Stage 2	Stage 3
Stage	• Autoimmunity • Normoglycemia • Presymptomatic	• Autoimmunity • Dysglycemia • Presymptomatic	• New-onset hyperglycemia • Symptomatic
Diagnostic criteria	• Multiple autoantibodies • No IGT or IFG	• Multiple autoantibodies • Dysglycemia: IFG and/or IGT • FPG 100–125 mg/dL (5.6–6.9 mmol/L) • 2-h PG 140–199 mg/dL (7.8–11.0 mmol/L) • A1C 5.7–6.4% (39–47 mmol/mol) or ≥10% increase in A1C	• Clinical symptoms • Diabetes by standard criteria

American Diabetes Association Standards of Medical Care in Diabetes.
Classification and diagnosis of diabetes. Diabetes Care 2017; 40 (Suppl. 1): S11-S24

American Diabetes Association.

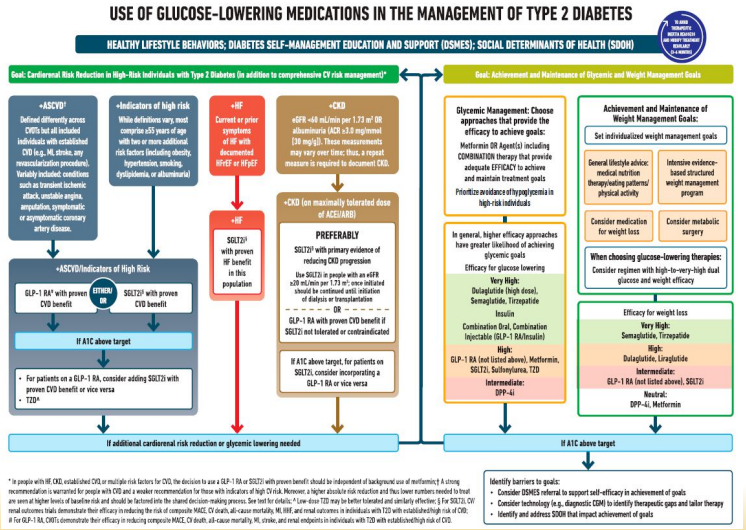
5

TYPE 1 DIABETES CAN AFFECT ANYONE, ANY AGE



Distribution of age at diagnosis in US adults with T1D (n=947), National Health Interview Survey (NHIS), 2016 to 2022. Adapted from Fang M. *Ann Intern Med.* 2023.

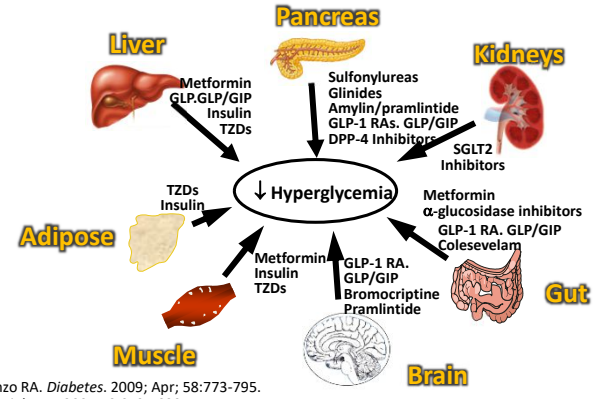
6



Pharmacologic Approaches to Glycemic Treatment: *Standards of Care in Diabetes - 2024. Diabetes Care* 2024;47(Suppl. 1):S158-S178

7

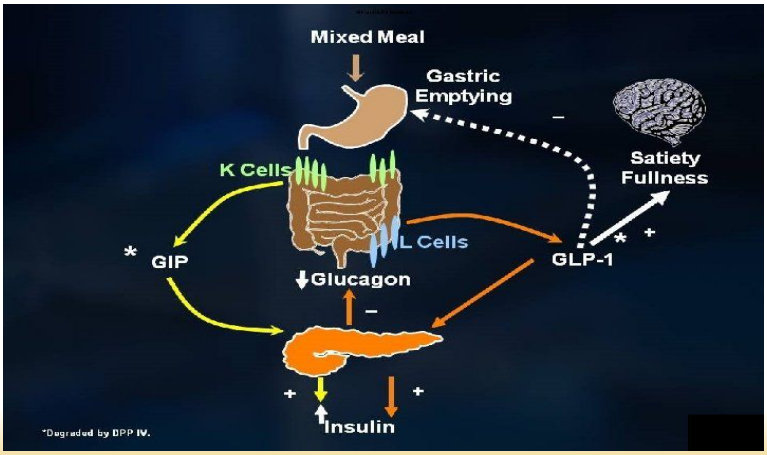
2024: AVAILABLE ANTIHYPERGLYCEMIC AGENTS



ADA 2024. DeFronzo RA. *Diabetes*. 2009; Apr; 58:773-795.
Holst JJ, Orskov C. *Diabetes*. 2004;53:S197-S204.
Lebovitz HE. *Diabetes Rev.* 1999;7:139-153.

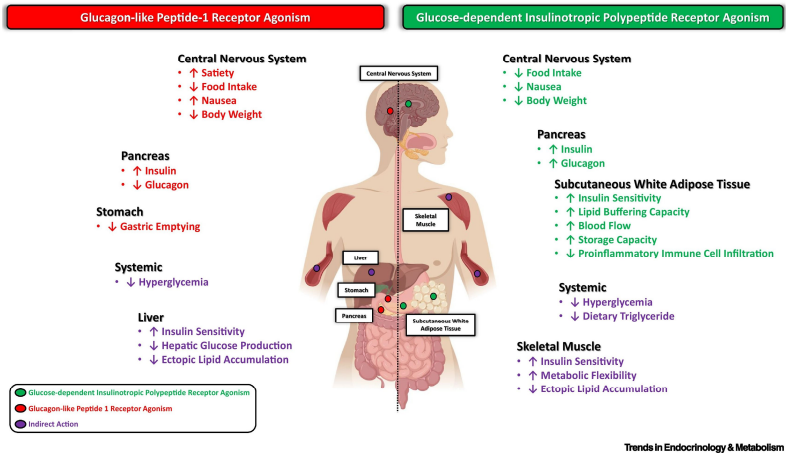
8

GLP1 AND GLP1/GIP



9

GLP1/GIP



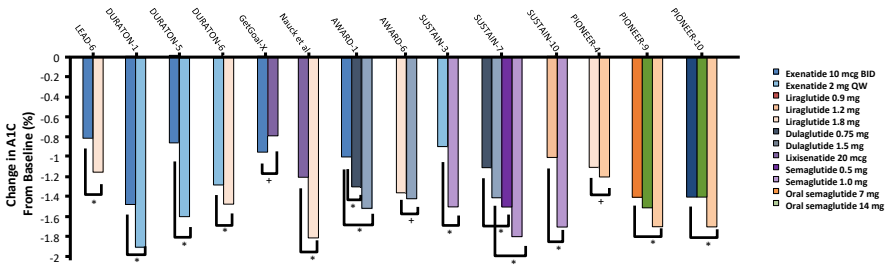
10

SEMAGLUTIDE APPROVALS

- Lowering of A1c
- Reduced risk of CV death, heart attack and stroke
- Slows progression of renal disease
- Improvement in sleep apnea
- Under investigation: dementia, addictions, lung disease, PCOs, MASLD

11

GLP-1 RA COMPARATIVE STUDIES: CHANGE IN A1C

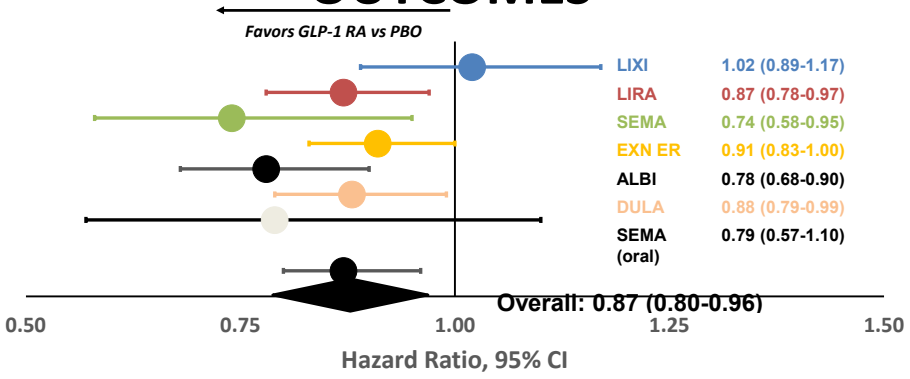


*P <0.05. †P <0.05, meeting predefined noninferiority margin.
Figure adapted from Trujillo. Ther Adv Endocrinol Metab. 2021;12:2042018821997320. Note that direct comparisons between clinical trials cannot be made.
Ahmann. Diabetes Care. 2018;41:258. Blevins. J Clin Endocrinol Metab. 2011;96:1301. Buse. Lancet. 2009;374:39. Buse. Lancet. 2013;381:117. Capehorn. Diabetes Metab. 2020;46:100-109. Drucker. Lancet. 2008;372:1240. Dungan. Lancet. 2014;384:1349. Nauck. Diabetes Care. 2016;39:1501. Pratley. Lancet. 2019;394:39-50. Pratley. Lancet Diabetes Endocrinol. 2018;6:275. Rosenstock. Diabetes Care. 2013;36:2945. Wysham. Diabetes Care. 2014;37:2159. Yabe. Lancet Diabetes Endocrinol. 2020;8:392-406. Yamada. Lancet Diabetes Endocrinol. 2020;8:377-391.

PCE 12

12

GLP-1 RA CVOTS: MACE[A] OUTCOMES[1]



[a] CV death, nonfatal myocardial infarction, and nonfatal stroke in all 7 trials, plus hospitalization for unstable angina in ELIXA.[2-8]

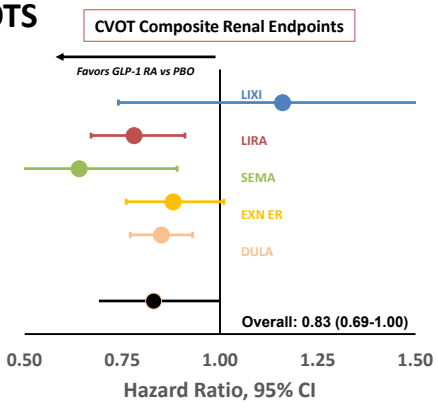
1. Giugliano D, et al. *Diabetes Obes Metab.* 2019;21:2576-2580; 2. Pfeffer MA, et al. *N Engl J Med.* 2015;373:2247-2257; 3. Marso SP, et al. *N Engl J Med.* 2016;375:311-322; 4. Marso SP, et al. *N Engl J Med.* 2016;375:1834-1844; 5. Holman RR, et al. *N Engl J Med.* 2017;377:1228-1239; 6. Hernandez AF, et al. *Lancet.* 2018;392:1519-1529; 7. Gerstein HC, et al. *Lancet.* 2019;394:121-130; 8. Husain M, et al. *N Engl J Med.* 2019;381:841-851.

13

HEART FAILURE AND RENAL FUNCTION EFFECTS IN GLP-1 RA CVOTS

- HF
  - Meta-analysis demonstrated a 9% reduction in the risk of hospitalization for HF for GLP-1 RAs as a class
  - No significant effects on HF were identified in individual trials
- Renal effects
  - Meta-analysis demonstrated a 17% reduction in composite kidney outcomes for GLP-1 RAs as a class
  - Renal benefit driven by reduction in macroalbuminuria (HR, 0.76 [0.68-0.86])

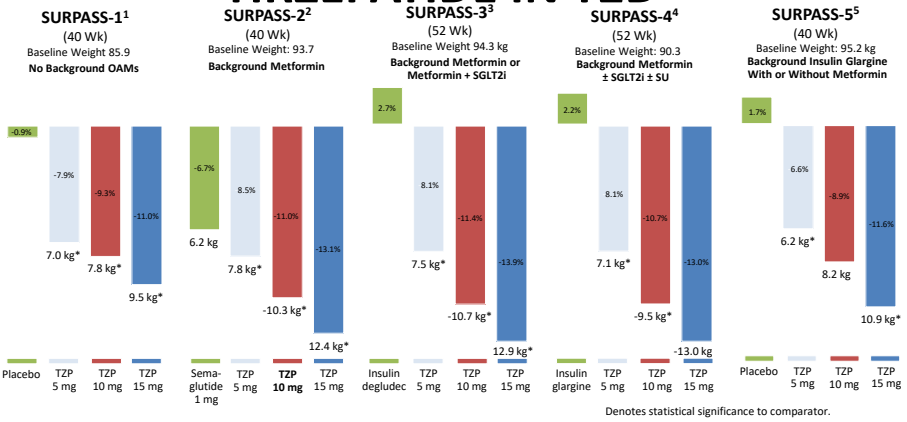
Semaglutide 1.0mg FDA approval for CKD January 2025. Based on the FLOW Trial. NEJM FLOW: Ozempic (semaglutide 1.0 mg) reduces risk of kidney disease-related events and MACE in people with T2D and CKD – big win for complication reduction – May 24, 2024



Giugliano D, et al. *Diabetes Obes Metab.* 2019;21:2576-2580.

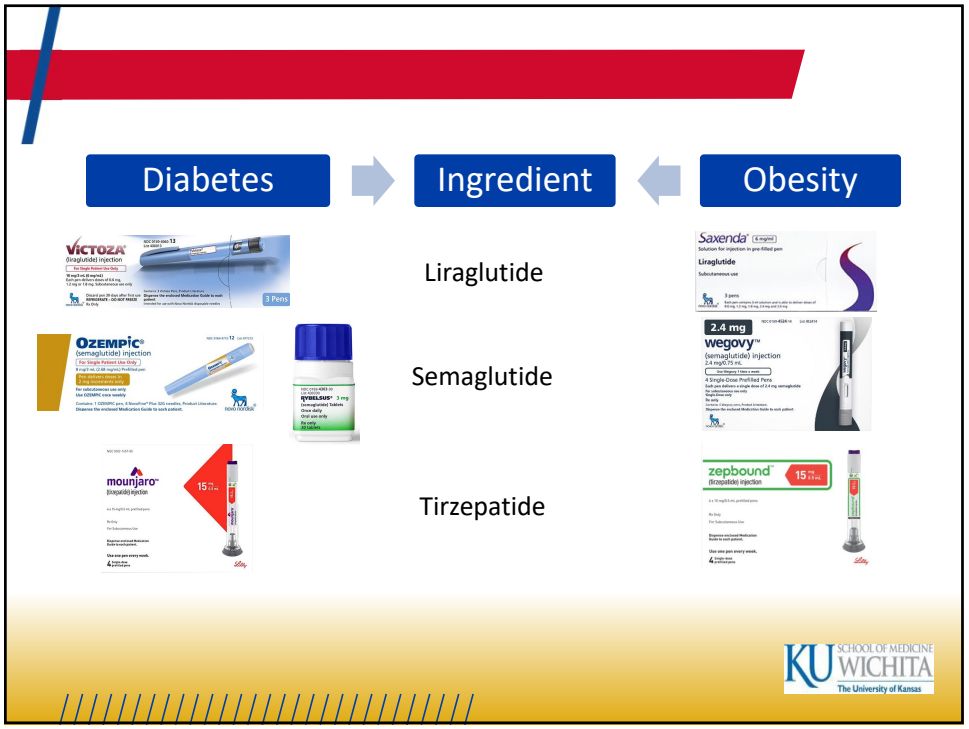
14

SURPASS: WEIGHT LOSS WITH TIRZEPATIDE IN T2D



1. Rosenstock. Lancet. 2021;398:143. 2. Frias. NEJM. 2021;385:503. 3. Giorgino. ADA 2021. Abstr 78-LB.
4. Del Prato. Lancet. 2021;398:1811. 5. Dahl. ADA 2021. Abstr 80-LB.

15



16

TERZEPATIDE/(MOUNJARO)

- GLP1/GIP agonist
- Once a week auto injector
- 2.5mg/5/mg/7.5mg/10mg/12.5mg/15mg per 0.5 mL
- Works on fasting and post meal glucose
- Helps you feel full, can contribute to weight loss (13-25lb)
- Potential Side effects: Nausea/Vomiting/↓ Appetite /Diarrhea or Constipation
  - Acute kidney diseases can occur if you get dehydrated
- Contraindicated: personal or family history of medullary thyroid carcinoma (MTC), or in patients with Multiple Endocrine neoplasia syndrome type 2 (MEN2),
- Risk of Thyroid c-cell tumors, acute pancreatitis, hypoglycemia if used with SU or Insulin (dose needs to be adjusted).
- A1c reduction 1.7-2.4%
- Cost: $$$, co-pay card

17

SEMAGLITIDE(OZEMPIC)

- GLP1 agonist
- Once a week multi-dose pen
- 2 mg in 1.5 mL, 4 mg / 3 mL, or 8 mg / 3 mL
- Works on fasting and post meal glucose
- Helps you feel full, can contribute to weight loss (average 14 # @ 10 months)
- Potential Side effects: Nausea/Vomiting/↓ Appetite /Diarrhea or Constipation
  - Acute kidney diseases can occur if you get dehydrated
- Contraindicated: personal or family history of medullary thyroid carcinoma (MTC), or in patients with Multiple Endocrine neoplasia syndrome type 2 (MEN2),
- Potential progression of retinopathy, acute pancreatitis, hypoglycemia if used with SU or Insulin (dose needs to be adjusted).
- A1c reduction 1.4-2.1%
- Cost: $$$, co-pay card

18

COMPARISONS

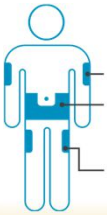
GLP-1RA and Dual GLP-1RA/GIP Injection Devices

	Use the links below each product for *"How to Use"* guides	Medications (Blue names are indicated for T2DM and green for obesity)	Pen Needles	Preparation	Stability at Room Temp
Single- Use (Hidden Needle)	 Trulicity, Mounjaro, Zepbound	Trulicity (dulaglutide)	N/A	None	14 days
		Mounjaro and Zepbound (tirzepatide)			21 days
	 Wegovy	Wegovy (semaglutide)	N/A	None	28 days
	 Bydureon	Bydureon BCise (exenatide ER)	N/A	➢ Must be at room temperature for >15min prior to injection ➢ Shake hard for 15 seconds to mix	28 days (MUST store flat on its side)
Multi-Use	 Ozempic, Victoza, Saxenda	Ozempic (semaglutide)	Included	➢ Attach pen needle and dial to appropriate dose	56 days
		Victoza and Saxenda (liraglutide)	NOT included		30 days

Beth Israel Lahey Health

19

- Medication Storage
  - Refrigerate until ready to use
    - Do not freeze
  - Can stay at room temperature for:
    - Liraglutide: 30 days after first use
    - Semaglutide: 28 days
    - Tirzepatide: 21 days
- Injection Tips
  - Select a new site each time
  - Use a new needle each time (Liraglutide, Semaglutide)



Upper arms

Stomach (keep 2 inches away from your belly button)

Upper legs (front of thighs)

- Disposal of Needles
  - Hard sided container
  - "Do Not Recycle- SHARPS"

KU SCHOOL OF MEDICINE WICHITA The University of Kansas

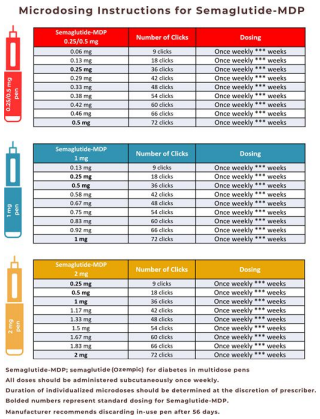
20

MITIGATING SIDE EFFECTS

- Set realistic expectations
- Go slow with dose titration
- Encourage mindful eating
- Stay hydrated

21

MICRODOSING SEMAGLUTIDE



Microdosing Instructions for Semaglutide-MDP

Semaglutide-MDP 0.25/0.5 mg	Number of Clicks	Dosing
0.06 mg	9 clicks	Once weekly *** weeks
0.13 mg	18 clicks	Once weekly *** weeks
0.25 mg	36 clicks	Once weekly *** weeks
0.29 mg	42 clicks	Once weekly *** weeks
0.33 mg	48 clicks	Once weekly *** weeks
0.38 mg	54 clicks	Once weekly *** weeks
0.42 mg	60 clicks	Once weekly *** weeks
0.46 mg	66 clicks	Once weekly *** weeks
0.5 mg	72 clicks	Once weekly *** weeks

Semaglutide-MDP 1 mg	Number of Clicks	Dosing
0.13 mg	9 clicks	Once weekly *** weeks
0.25 mg	18 clicks	Once weekly *** weeks
0.5 mg	36 clicks	Once weekly *** weeks
0.58 mg	42 clicks	Once weekly *** weeks
0.67 mg	48 clicks	Once weekly *** weeks
0.75 mg	54 clicks	Once weekly *** weeks
0.83 mg	60 clicks	Once weekly *** weeks
0.92 mg	66 clicks	Once weekly *** weeks
1 mg	72 clicks	Once weekly *** weeks

Semaglutide-MDP 2 mg	Number of Clicks	Dosing
0.25 mg	9 clicks	Once weekly *** weeks
0.5 mg	18 clicks	Once weekly *** weeks
1 mg	36 clicks	Once weekly *** weeks
1.17 mg	42 clicks	Once weekly *** weeks
1.33 mg	48 clicks	Once weekly *** weeks
1.5 mg	54 clicks	Once weekly *** weeks
1.67 mg	60 clicks	Once weekly *** weeks
1.83 mg	66 clicks	Once weekly *** weeks
2 mg	72 clicks	Once weekly *** weeks

Semaglutide-MDP; semaglutide (Ozempic) for diabetes in multidose pens
All doses should be administered subcutaneously once weekly.
Duration of individualized microdoses should be determined at the discretion of prescriber.
Bolded numbers represent standard dosing for Semaglutide-MDP.
Manufacturer recommends discarding in-use pen after 56 days.

https://diabetesjournals.org/care/article/48/3/e25/157716/One-Size-Does-Not-Fit-All-Understanding

22

PREVENTION OF HYPOGLYCEMIA

- Slow onset of med BUT consider lowering insulin doses
- Observation: effects prandial insulin first and most
- As weigh loss occurs basal dose lowering
- CGM is very helpful in guiding lowering of insulin
- NO need and should never be on GLP1/GIP and DPP4
- Likely stop SU and or at minimum lower it

23

PATIENT CONSIDERATION

- Women lose more than men
- In diabetes, weight loss is not only goal, caution with older patients, may not want to increase doses to prevent excessive weight loss
- Approximately ½ to 2/3 of weight may be regained with med stoppage
- 10% may not have weight loss but other benefits

24

SURGERY/PROCEDURE CONSIDERATIONS

- **Multisociety Clinical Practice Guidance for GLP1 Receptor Agonist in Perioperative Period**
  - Rec 1-elevated risk of delayed gastric emptying
    - Highest risk in escalation phase, higher doses, weekly dosing vs daily, presence of gastric symptoms, medical conditions: bowel dysmobilty, gastroparesis, Parkinson's
    - Continue med if without elevated risk
    - Balance risk of hazardous metablolic state like hyperglycemia
    - If determined need to stop, stop weekly 1 week prior and daily, day prior
  - Rec 2-If concerned
    - Perioperative liquid diet 24 hours prior to procedure
    - If concerned and available do point of care gastric ultrasounds
    - Engage in shared decision making on risk (studies are variable regarding risk)

Chang MG et all J Clin Med Oct 2024, 13(21)
Kindal T et call (2024)

25

DOSE COMPARISON

Drug (Brand Name)	Frequency	Dose 1	Dose 2	Dose 3	Dose 4
Dulaglutide (Trulicity)*	Weekly	0.75 mg	1.5 mg	3 mg**	4.5 mg**
Semaglutide (Ozempic)*	Weekly	0.25 mg†	0.5 mg	1 mg	2 mg
Liraglutide (Victoza)*	Daily	0.6 mg†	1.2 mg	1.8 mg	-
Oral Semaglutide (Rybelsus)	Daily	3 mg†	7 mg	14 mg	-
Exenatide (Bydureon BCise)‡	Weekly	2 mg	-	-	-
Exenatide (Byetta)§	Twice Daily	5 mcg	10 mcg	-	-
Tirzepatide (Mounjaro)¶	Weekly	2.5 mg†	5 mg	7.5 mg	10 mg

26

EXERCISE/PHYSICAL ACTIVITY

- Glycemic response to various exercise types
  - Aerobic
    - Usually results in decrease in blood glucose
    - Most often within the first 45 minutes
    - Intense activity will increase rise of lows 6 to 12 hours later
  - Resistance training (powerlifting, sprints)
    - Glucose levels frequently rise
  - High intensity interval training
    - Glucose levels frequently rise
    - Will rise especially if high glucose prior to activity

27

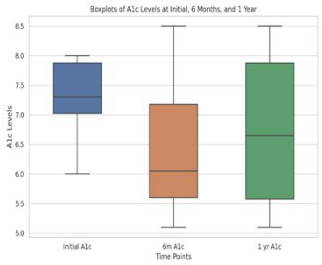
MEAL PLANNING CONSIDERATIONS

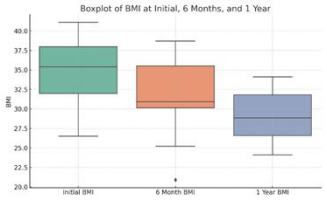
- Prevent Muscle loss
- Counsel appropriate protein in meal plan
  - 1 to 1.5 gm/kg (80 to 150 grams per day)
  - Chicken, fish, beans, lentils, low fat diary, nuts, eggs
- Adequate calories
  - At least 1300 to 1500 calories per day

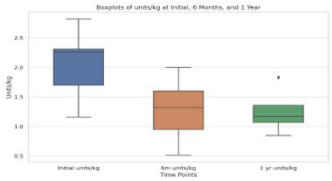
28

TYPE 1 DIABETES

- Has been used
- USE caution







Arturk HK 2024, Childs B et al 2024

29

GREAT PLAINS DIABETES CENTER

BELINDA "LINDY" CHILDS, APRN-CNS, BC-ADM, CDCES
834 N. SOCORA, SUITE 4
WICHITA, KANSAS 67212
PHONE 316-440-2802
FAX 316-440-2809
EMAIL:INFO@GREATPLAINSDIABETES.COM

30

REFERENCES

- Anne M. Komé, Mary M. Chandran, Shelby S. Tungate Lopez, John B. Buse, Klara R. Klein; One Size Does Not Fit All: Understanding Microdosing Semaglutide for Diabetes in Multidose Pens. *Diabetes Care* 20 February 2025; 48 (3): e25–e27. https://doi.org/10.2337/dc24-2575
- Van Dril E, Allison M, Schumacher C. Deprescribing in type 2 diabetes and cardiovascular disease: Recommendations for safe and effective initiation of glucagon-like peptide-1 receptor agonists in patients on insulin therapy. Am Heart J Plus. 2022 Jul 2;17:100163. doi: 10.1016/j.ahjo.2022.100163. PMID: 38559880; PMCID: PMC10978364
- https://www.talktomira.com/post/can-i-switch-between-semaglutide-ozempic-and-tirzepatide-mounjaro
- Wharton S, Davies M, Dicker D, Lingvay I, Mosenzon O, Rubino DM, Pedersen SD. Managing the gastrointestinal side effects of GLP-1 receptor agonists in obesity: recommendations for clinical practice. Postgrad Med. 2022 Jan;134(1):14-19. https://pubmed.ncbi.nlm.nih.gov/34775881/
- Chang MG, Ripoll JG, Lopez E, Krishnan K, Bittner EA. A Scoping Review of GLP-1 Receptor Agonists: Are They Associated with Increased Gastric Contents, Regurgitation, and Aspiration Events? J Clin Med. 2024 Oct 23;13(21):6336. doi: 10.3390/jcm13216336. PMID: 39518474; PMCID: PMC11546377.
- Multisociety Clinical Practice Guidance for the Safe Use of Glucagon-like Peptide-1 Receptor Agonists in the Perioperative Period, Kindel, Tammy L. et al. (2024), Clinical Gastroenterology and Hepatology, https://www.cghjournal.org/article/S1542-3565(24)00910-8/fulltext#collab0020
- Akturk HK, Dong F, Snell-Bergeon JK, Karakus KE, Shah VN. Efficacy and Safety of Tirzepatide in Adults With Type 1 Diabetes: A Proof of Concept Observational Study. Journal of Diabetes Science and Technology. 2024;0(0). doi:10.1177/19322968231223991