Medications for Type 2 Diabetes

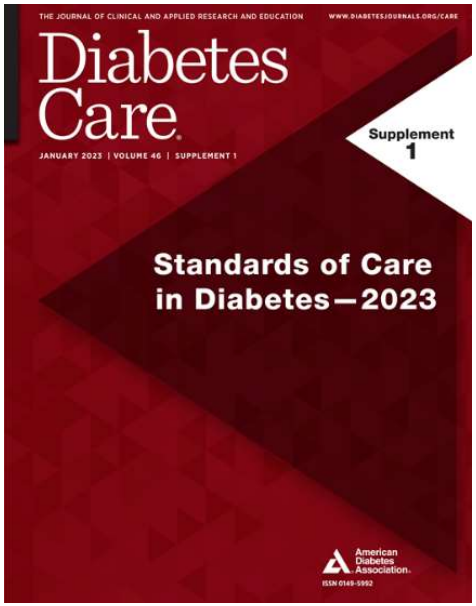
Beverly Dyck Thomassian, RN, MPH, BC-ADM, CDCES
President, Diabetes Education Services
www.DiabetesEd.net

Diabetes Meds for Type 2:

1. Describe the main action of the different categories of type 2 diabetes medications.
2. Discuss strategies to determine the right medication for the right patient.
3. List the side effects and clinical considerations of each category of medication.

Coach Bev has no conflicts of interest

- Not on any speaker's bureau
- Does not invest in pharmaceutical or device companies
- Gathers information from reading package inserts, research and standards



Majority of content from ADA Standards
www.Diabetes.org

Standard 9

ADA & European Association for the Study of Diabetes (EASD) Consensus Management of Hyperglycemia in Type 2

ıthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB
7/dci22-0034. *Diabetologia* 2022; https://doi.org/10.1007/s00125-022-05787-2.

Poll Question 1

- 1. Which factors are most important to consider matching meds to individuals?

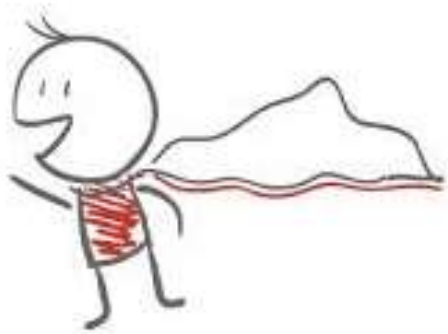
  a. Insurance coverage

  b. Heart and kidney health

  c. Willingness to take meds

  d. Persons values and preferences

  e. all of the above



Person Centered Approach

"...providing care that is respectful of and responsive to individual patient preferences, needs, and values - ensuring that patient values guide all clinical decisions."

- **Gauge patient's preferred level of involvement.**
- **Explore, where possible, therapeutic choices.**
- **Utilize decision aids.**

- **<u>Shared</u> decision making – final decisions re: lifestyle choices ultimately lie with the indvidual.**

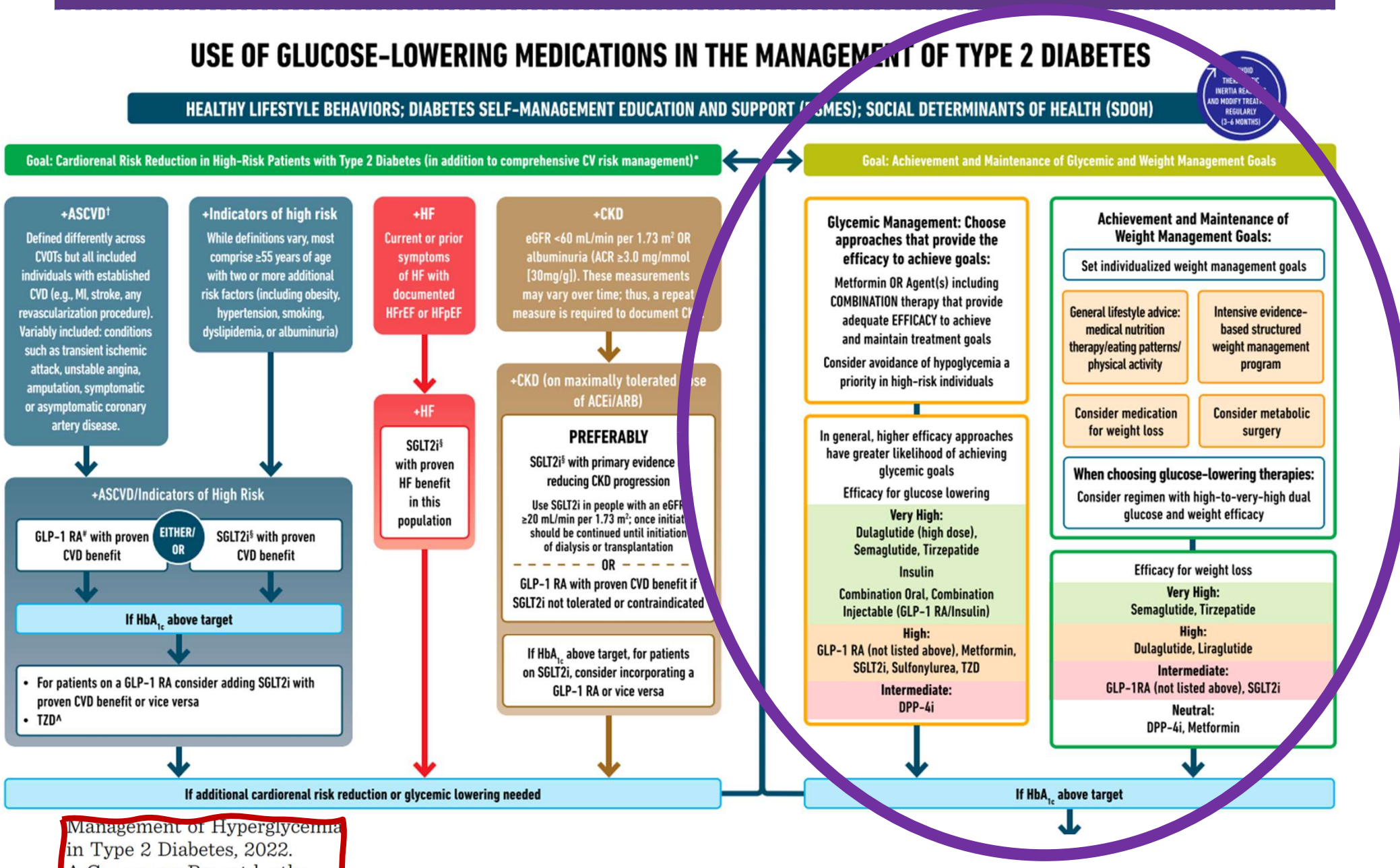
ADA-EASD Position Statement: Management of Hyperglycemia in T2DM – updated in 2015

Antihyperglycemic Therapy Steps

- Medication choice based on individual
- All individuals receive ongoing coaching to work toward positive Lifestyle Changes
  - Healthy eating
  - Activity

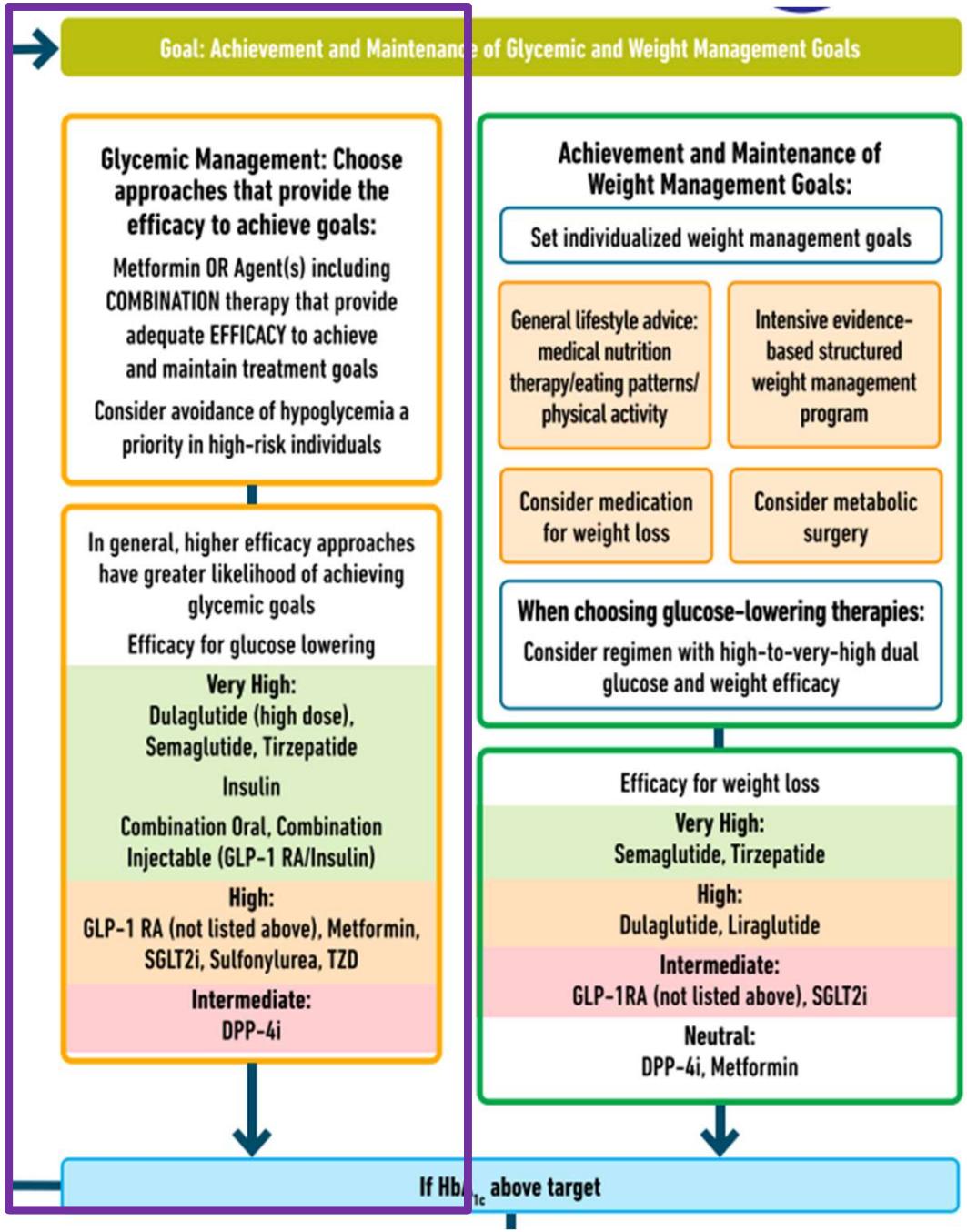
Shared-decision making each step of the way

ADA Meds Management



Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the

Metformin is "Usually" 1st Line



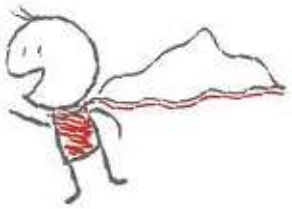
- Why metformin?
  - Longstanding evidence
  - High efficacy and safety
  - Inexpensive - 3 months for $12
  - Weight neutral

- If ASCVD, HF or CKD or high ASCVD risk, use SGLT2i or GLP-1 RA +/- metformin
- If A1C ≥ 8.5%, consider combo therapy.

Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the

Poll Question 2

- What are qualities of an ideal diabetes medication?



a. No weight gain or some weight loss

b. Increases UACR and decreases GFR

c. Only causes hypoglycemia once a week

d. Reduce cardiorenal risk

e. A and D

Ideal Diabetes Med -

- No hypoglycemia
- No weight gain
- Affordable
- Lowers cardiorenal risk
- Most people can tolerate /use?

Poll Question 3

- 59 yrs, type 2, with BMI of 29, A1c 8.4, GFR 62. Their formulary covers the following medications. What 1st class of med would you suggest?

  a. Sulfonylureas

  b. Biguanides - Metformin

  c. DPP-IV Inhibitors

  d. Insulin

  e. TZD (Actos)

Common Oral Diabetes Meds

Diabetes Education SERVICES

Class/Main Action	Name(s)	Daily Dose Range	Considerations
Biguanides • Decreases hepatic glucose output • First line med at diagnosis of type 2	metformin (Glucophage) Riomet (liquid metformin)	500 - 2550 mg (usually BID w/ meal) 500 - 2550 mg 500mg/5mL	**Side effects:** nausea, bloating, diarrhea, B12 deficiency. To minimize GI Side effects, use XR and take w/ meals. **Obtain GFR before starting.** • If GFR <30, do not use. • If GFR <45, don't start Meformin • If pt on Metformin and GFR falls to 30-45, eval risk vs. benefit; consider decreasing dose. **For dye study,** if GFR <60, liver disease, alcoholism or heart failure, restart metformin after 48 hours if renal function stable. **Benefits:** lowers cholesterol, no hypo or weight gain, cheap. Approved for pediatrics, 10 yrs + Lowers A1c 1.0%-2.0%.
	Extended Release-XR (Glucophage XR) (Glumetza) (Fortamet)	(1x daily w/dinner) 500 – 2000 mg 500 – 2000 mg 500 – 2500 mg	

Biguanide derived from:
Goat's Rue *Galega officinalis*,
French Lilac
Does NOT harm kidneys
$10 for 3-month supply from
Walmart & other pharmacies

Biguanides - Metformin

- Benefits
  - Decrease LDL cholesterol and triglycerides
  - No weight gain, possible modest weight loss
  - Cancer protective?
- Concerns
  - Diarrhea and abdominal discomfort – Use XR
  - Lactic acidosis if improperly prescribed
  - Watch for B12 deficiency – ask about neuropathic pain

Teaching Tips

- Ask about diarhhea, switch to XR
- Doesn't damage kidneys.

Metformin – How does it rate?

Question	Answer
Cause hypoglycemia?	No
Cause weight gain?	No
Affordable?	Yes
Lowers CV risk?	Yes
Can most tolerate /use?	Yes/No (GI, GFR)

When goal is to minimize cost

- Go generic. Metformin and Sulfonylureas
- Walmart, Target others offers 3 month supply of following meds for ~ $10
  - Metformin and Metformin XR
  - Glipizide, Glyburide, Glimepiride
- Other generics include:
  - AWP – average wholesale price month
  - Actos (for steatosis, post stroke $5
  - Acarbose, Nateglinide, Repaglinide $30
  - More cost info – ADA Standards 2023

How much do they cost?

- Which of the following groups of meds for a month supply are cheapest? (multiple)

a. Actos and Avandia $5 & $324

b. Glipizide, Glyburide, Glimepiride $10 for 3 mo's

c. Metformin and Metformin XR $10 for 3 mo's

d. Januvia and Onglyza (DPP-IVs) $596 & $549

e. Exenatide and Semaglutide (GLP-1 RA's) $909, $1022

f. Empagliflozin and SGLT-2s $600- $700

g. Tirzepatide (Mounjaro) (GLP-1 + GIP) $974

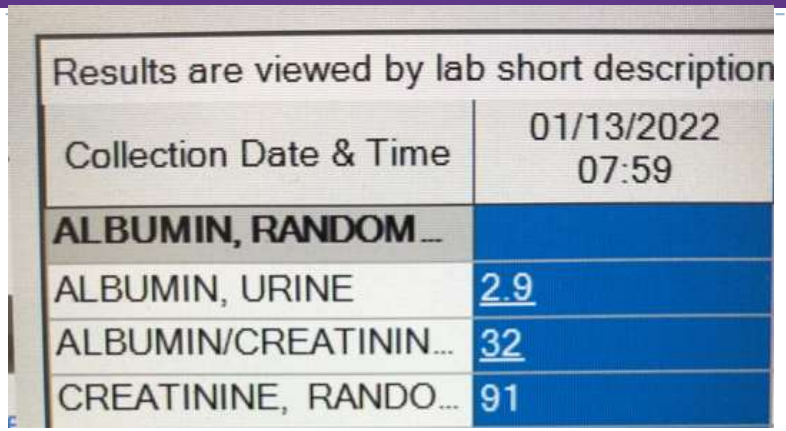
See ADA Standards on Median Monthly Average Wholesale Price (AWP) 2023

Life Study

- 69-year-old with BMI of 26, type 2 diabetes for past 3 years. Has been trying to manage diabetes with diet and exercise. GFR 32, UACR 46 mg/g.
- Most recent A1c 8.4%
- Limited income, pays cash for meds.
- What is the significance of GFR and UACR?

Evaluating Kidney Function - Albumin

- Urinary Albumin Creatinine Ratio (UACR)
- UACR can be assessed with a urinary spot collection.
  - Evaluates ratio of urine albumin /creatinine in mg/g
  - Target range < 30mg/g
  - If elevated, repeat test to verify
- Check at diagnosis in T2D and within 5 years in T1D



Results are viewed by lab short description	
Collection Date & Time	01/13/2022 07:59
ALBUMIN, RANDOM...	
ALBUMIN, URINE	2.9
ALBUMIN/CREATININ...	32
CREATININE, RANDO...	91

2.9 / 91 = 0.0318 mg/mg or 31.8 (32) in mg/g

Albuminuria Categories	Urinary Albumin Creatine Ratio (UACR)
Normal to mildly increased – A1	< 30 mg/g
Moderately increased – A2	30 – 299 mg/g
Severely increased – A3	300 mg/g +

Evaluating Kidney Function - GFR

- Glomerular Filtration Rate (GFR)– target is 60 or greater
  - Stage 3 indicates progressive renal failure
    - GFR 30 to 59
  - Stage 4 and 5 indicates severe loss and failure
    - GFR 29 or less

Kidney Disease Stage	GFR
Stage 1 – Normal	90+
Stage 2 – Mild loss	89 - 60
Stage 3a – Mild to Mod	59 - 45
Stage 3b – Mod to Severe	44 - 30
Stage 4 – Severe loss	29 -15
Stage 5 – Kidney failure	14 - 0

Life Study

- 69-year-old with BMI of 26, type 2 diabetes for past 3 years. Has been trying to manage diabetes with diet and exercise. GFR 32, UACR 46 mg/g.
- Most recent A1c 8.4%
- Limited income, pays cash for meds.
- What class are you considering?

Sulfonylureas –

- Action: tells pancreas to squirt insulin all day
- Efficacy:
  - Decrease FPG 60-70 mg/dl
  - Reduce A1C by 1.0-2.0%

Sulfonylureas

- Mechanism: Stimulate beta cells to release insulin
- Dosed 1-2x daily before meals
- Adverse effects
  - Hypoglycemia, Weight gain, watch renal function
- Low cost, $12 for 3 months supply
- Can help with glucose toxicity

Sulfonylureas • Stimulates sustained insulin release	glyburide: (Diabeta) (Glynase PresTabs)	 1.25 – 20 mg 0.75 – 12 mg	Can take once or twice daily before meals. Low cost generic. **Side effects**: hypoglycemia and weight gain. Eliminated via kidney. **Caution**: Glyburide most likely to cause hypoglycemia. Lowers A1c 1.0% – 2.0%.
	glipizide: (Glucotrol) (Glucotrol XL)	2.5 – 40 mg 2.5 – 20 mg	
	glimepiride (Amaryl)	1.0 – 8 mg	

Sulfonylureas

- Other Effects
  - Hypoglycemia
  - Weight gain
  - Cleared by kidney, use caution for ind's with kidney problems
  - Cheap
  - Can be helpful in presence of glucose toxicity

Life Study

- 69 year old with BMI of 26, type 2 diabetes for past 3 years. Has been trying to manage diabetes with diet and exercise.
  GFR 32, UACR 46 mg/g.
- Most recent A1c 8.4%
- Limited income, pays cash for meds.

- What class are you considering?
  - Can't start metformin due to low GFR.
  - Start 5-10 mg daily glipizide with glucose monitoring

Squirters – How does they rate?

Question	Answer
Cause hypoglycemia?	Yes
Cause weight gain?	Yes
Affordable?	Yes
Lowers CV risk?	No
Can most tolerate /use?	Yes/No

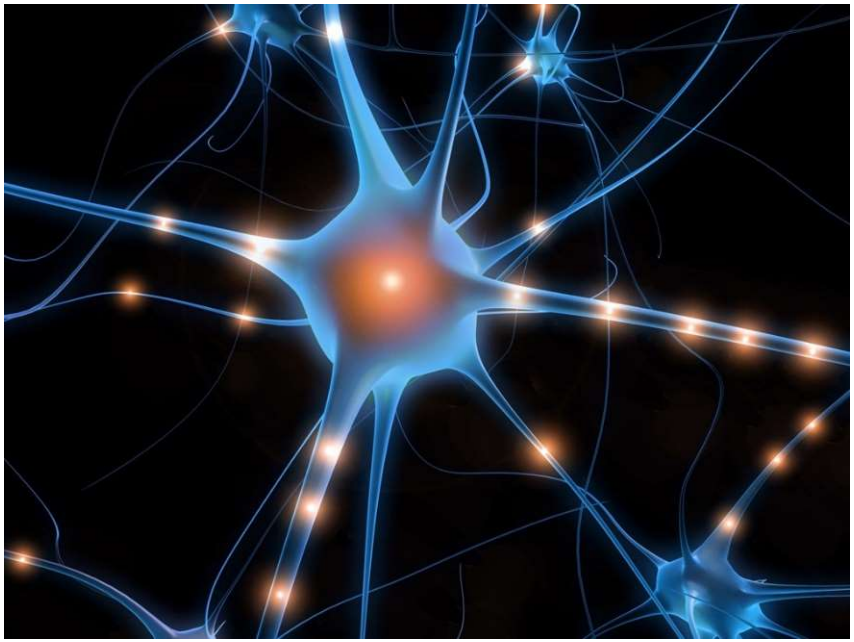
Poll 4 - Struggling with weight

44-year-old on Metformin and Sulfonylurea, A1c 8.4. Struggling with weight. Possible next options?

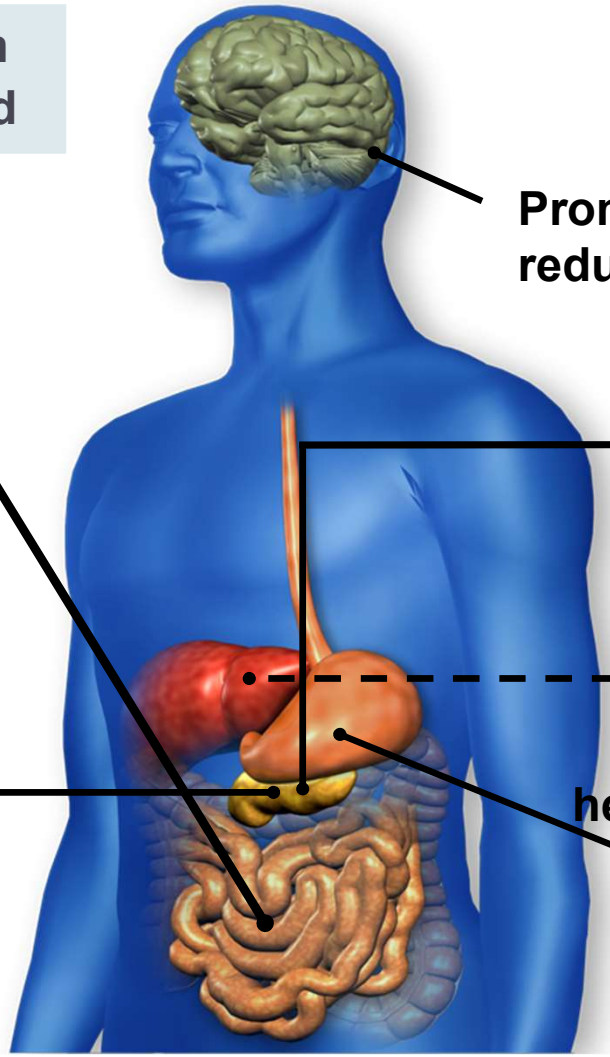
a. Refer to RD / RDN
b. Suggest addition of GLP-1 Agonist
c. Increase dose of sulfonylurea
d. Suggest starting insulin
e. A and B

Incretin Mimetics – "Gut Hormone Imitators" GLP-1 & GLP-1/GIP Agonists

- How do they work?



GLP-1 Effects in Humans
Understanding the Natural Role of Incretins



GLP-1 secreted upon the ingestion of food

↑ Beta-cell response

Promotes satiety and reduces appetite

Alpha cells:
↓ Postprandial glucagon secretion

Liver:
↓ Glucagon reduces hepatic glucose output

Beta cells:
Enhances glucose-dependent insulin secretion

Stomach:
Helps regulate gastric emptying

GLP-1 degraded by DPP-4 w/in minutes

Adapted from Flint A, et al. *J Clin Invest*. 1998;101:515-520
Adapted from Larsson H, et al. *Acta Physiol Scand.* 1997;160:413-422
Adapted from Nauck MA, et al. *Diabetologia*. 1996;39:1546-1553
Adapted from Drucker DJ. *Diabetes*. 1998;47:159-169

GLP-1 & GIP Receptor Agonists

Class/Main Action	Name	Dose Range	Considerations
GLP-1 RA - Glucagon Like Peptide Receptor Agonist **"Incretin Mimetic"** • Increases insulin release with food • Slows gastric emptying • Promotes satiety • Suppresses glucagon	exenatide (Byetta)	5 and 10 mcg BID	**Side effects for all:** Nausea, vomiting, weight loss, injection site reaction. Report signs of acute pancreatitis or intestinal blockage (ileus) and stop med. Increase dose monthly to achieve targets. **Black box warning:** Thyroid C-cell tumor warning (avoid if family history of medullary thyroid tumor). *Significantly reduces risk of CV death, heart attack, and stroke. †Approved for pediatrics 10-17 yrs Lowers A1C 0.5 – 1.6% Weight loss: 4-6% body weight loss.
	exenatide XR† (Bydureon)	2 mg 1x a week Pen injector - Bydureon BCise	
	liraglutide (Victoza)*†	0.6, 1.2 and 1.8 mg daily	
	dulaglutide* (Trulicity)†	0.75, 1.5, 3.0 and 4.5 mg 1x a week pen injector	
	semaglutide* (Ozempic)	0.25, 0.5, 1.0 and 2.0 mg 1x a week pen injector	
	(Rybelsus) Oral tablet	3, 7, and 14 mg daily in a.m. Take on empty stomach with sip of water	
GLP-1 & GIP Receptor Agonist Activates receptors for GLP-1 (see above) & Glucose-dependent Insulinotropic Polypeptide (GIP).	Tirzepatide (Mounjaro)	2.5, 5.0, 7.5, 10, 12.5 and 15 mg 1x a week prefilled single dose pen Increase dose by 2.5 mg once monthly to reach targets.	**Side effects:** nausea, diarrhea, injection site reaction. Report pancreatitis, signs of intestinal blockage. **Black box warning:** Avoid if family history of medullary thyroid tumor. Lowers A1C ~ 1.8 - 2.4% Weight loss: 7-13% body weight loss at max dose.

Incretin Mimetics
Exenatide (Byetta)

- **Action:**
  - Insulin release in response to meal
  - Slows gastric emptying
  - Causes Satiety
- **Exenatide Dosing:**
  - 5-10 mcg before break, dinner
  - Pancreatitis Warning
- **Efficacy:** Decreases A1c by 0.7%, wt by 3lbs
- **Indication**: For type 2s only - mono or in combo
- 

Incretin Mimetics – Exenatide XR - Bydureon

- **Once a Week Dosing**: 2mg
- **Efficacy:** Decreases A1c by 1.6%, wt by ~6lbs
- **Indication**: For type 2s only. Approved for Peds 10+
- **Other**: – Available in pen / injector
- **Caution**:
  - not indicated for pt's w/ history of medullary thyroid tumor
  - pancreatitis warning

Incretin Mimetics - GLP-1 Analog
dulaglutide (Trulicity)

Dulaglutide Dosing: 0.75/ 1.5 /3.0 / 4.5 mg weekly

- **Efficacy:**
  lowers; A1c by ~ 1%,
  body wt by ~ 2.5kg
- **Indication**: Type 2 Monotherapy or in combo.
- **Reduces risk of CV events. Peds Approved**
- **Other**: single-dose pen, does not require mixing, measuring or needle attachment.
- Needle is hidden from the user and retracts after use.
- **Black box**–thyroid tumor warning (avoid if family hx, notify MD of hoarseness, lump).

Incretin Mimetics – Semaglutide (Ozempic)

- **Once a Week Dosing**: 0.5 – 2.0mg
- **Efficacy:**
  reduced hemoglobin A1c by 1.5 to 1.8% points.
- **4.5- to 6.4-kg weight loss.**
- **Reduces risk of CV events**
- **Side effects**: nausea, which diminished over time. Report signs of pancreatitis
- **Black box**–thyroid tumor warning (avoid if family hx, notify MD of hoarseness, lump).

Oral Semaglutide (Rybelsus)

- Dose: 3, 7 and 14 mg daily
- Take daily at least 30 mins before first food, beverage, or other oral meds
- Take with no more than 4 ounces of plain water
- Swallow tablets whole (don't cut or crush)
- Dosing:
  - Start with 3 mg once daily for 30 days
  - Then increase to 7mg once daily for 30 days
  - If A1c at target, maintain at 7mg daily
  - If A1c not at target, increase to 14 mg once daily

Incretin Mimetics - GLP-1 Analog
Liraglutide (Victoza)

Liraglutide Dosing: 1x daily, time not critical

- 0.6 x 1 week – if tolerated (nausea), go to >
- 1.2 x 1 week – then go to >
- 1.8 mg daily

- **Efficacy:** lowers; A1c by 1%, body wt by ~ 2.5kg.
  Reduces risk of CV events
- **Indication**: Monotherapy or in combo . Type 2 only
- **Other**: Pancreatitis warning
- Approved for Pediatrics 10+

Black box–thyroid tumor warnin
of hoarseness, lump).

GLP-1 RA Approved for Weight Loss

- Saxenda and Victoza same active ingredient (liraglutide) at different doses
  - Saxenda 3 mg (Victoza 1.8 mg)
  - 6% wt loss, $1619 a month
- Wegovy and Ozempic same active ingredient (semaglutide) at different doses
  - Wegovy 2.4mg (Ozempic 2mg)
  - 6% wt loss, $1619 a month

- Both are FDA approved as a treatment option for chronic weight management in addition to a reduced calorie diet and physical activity.
- Approved for use in adults with a
  - BMI of ≥ 30 or
  - BMI of ≥ 27 or greater who have hypertension, type 2 diabetes, or dyslipidemia.

GLP-1 & GIP Receptor Agonists

Class/Main Action	Name	Dose Range	Considerations
GLP-1 RA - Glucagon Like Peptide Receptor Agonist **"Incretin Mimetic"** • Increases insulin release with food • Slows gastric emptying • Promotes satiety • Suppresses glucagon	exenatide (Byetta)	5 and 10 mcg BID	**Side effects for all:** Nausea, vomiting, weight loss, injection site reaction. Report signs of acute pancreatitis or intestinal blockage (ileus) and stop med. Increase dose monthly to achieve targets. **Black box warning:** Thyroid C-cell tumor warning (avoid if family history of medullary thyroid tumor). *Significantly reduces risk of CV death, heart attack, and stroke. †Approved for pediatrics 10-17 yrs Lowers A1C 0.5 – 1.6% Weight loss: 4-6% body weight loss.
	exenatide XR† (Bydureon)	2 mg 1x a week Pen injector - Bydureon BCise	
	liraglutide (Victoza)*†	0.6, 1.2 and 1.8 mg daily	
	dulaglutide* (Trulicity)†	0.75, 1.5, 3.0 and 4.5 mg 1x a week pen injector	
	semaglutide* (Ozempic)	0.25, 0.5, 1.0 and 2.0 mg 1x a week pen injector	
	(Rybelsus) Oral tablet	3, 7, and 14 mg daily in a.m. Take on empty stomach with sip of water	
GLP-1 & GIP Receptor Agonist Activates receptors for GLP-1 (see above) & Glucose-dependent Insulinotropic Polypeptide (GIP).	Tirzepatide (Mounjaro)	2.5, 5.0, 7.5, 10, 12.5 and 15 mg 1x a week prefilled single dose pen Increase dose by 2.5 mg once monthly to reach targets.	**Side effects:** nausea, diarrhea, injection site reaction. Report pancreatitis, signs of intestinal blockage. **Black box warning:** Avoid if family history of medullary thyroid tumor. Lowers A1C ~ 1.8 - 2.4% Weight loss: 7-13% body weight loss at max dose.

Actions of GLP-1 and GIP

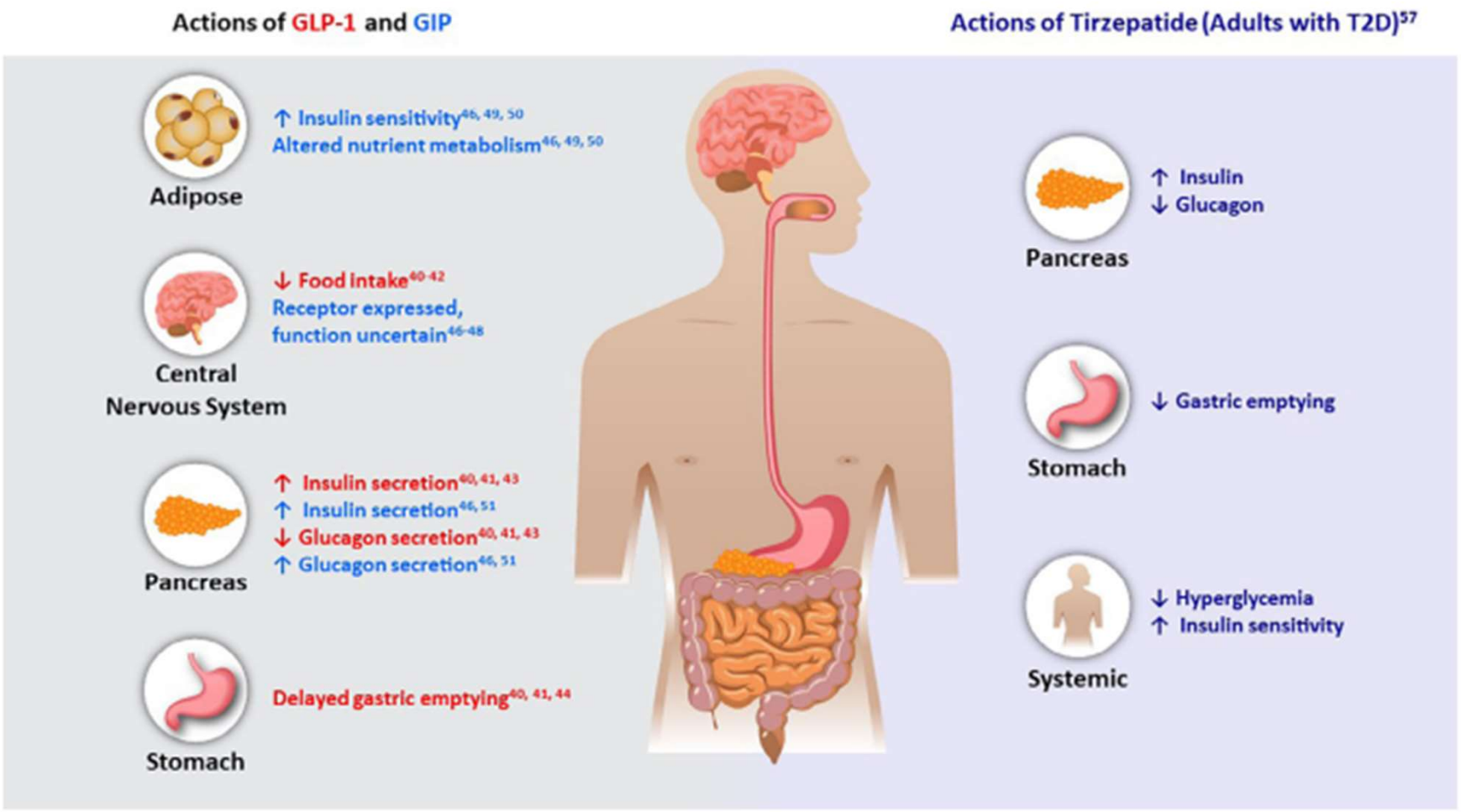


FIGURE 1 Gluco-regulatory actions of GIP and GLP-1 proposed based on preclinical and clinical studies, and actions of tirzepatide in adults with type 2 diabetes. GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide-1; T2D, type 2 diabetes

Received: 19 May 2022 | Revised: 26 July 2022 | Accepted: 2 August 2022
DOI: 10.1111/dom.14831

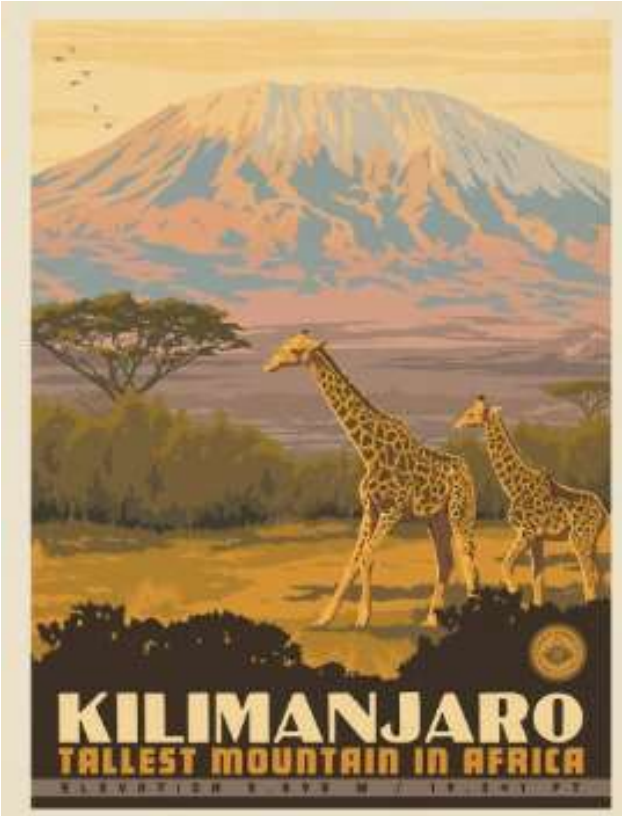
REVIEW ARTICLE

WILEY

Tirzepatide for the treatment of adults with type 2 diabetes: An endocrine perspective

GIP/GLP-1 Receptor Agonist

- Tirzepatide (Mounjaro) is a GIP/GLP-1 Receptor Agonist
  - GIP: glucose-dependent insulinotropic polypeptide
  - GLP-1: glucagon like peptide-1
- Studied in the SURPASS clinical program (T2DM)
- Studied in the SURMOUNT clinical program (Obesity)
- Once weekly injectable disposable pen: abdomen, legs, arms
- FDA approved for T2DM: May, 2022



Tirzepatide Wt loss and A1C impact

- A1C drop in Surpass Trials of
- 1.9% to 2.6%

- Weight loss in Surpass Trials of
- 7.8% to 12.9% or
- 13.6 to 28.4 pounds

- Approved as wt loss medication in 11/23. “Zepbound”

Tirzepatide (Mounjaro) Clinical Use

Starting dose (for 4 weeks)

MONTH 1

For at least 4 weeks

MONTH 2

IF ADDITIONAL GLYCEMIC CONTROL IS NEEDED

For at least 4 weeks

For at least 4 weeks

For at least 4 weeks

Maximum dose

Benefits of GLP-1 RA & GIP/GLP-1 Receptor Agonists

A1C lowering

Substantial Weight loss

Cardiovascular benefits*

Decrease appetited

Lowers post meal glucose

Ease of use

*semaglutide, liraglutide, dulaglutide

Poll Question 5

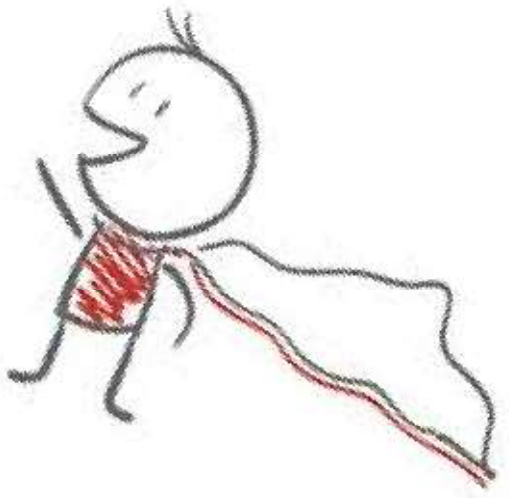
- RT is taking tirzepatide (Mounjaro) once weekly for 3 months. Which side effect should they report immediately?

  a. sneezing fits

  b. constipation

  c. headaches

  d. sudden abdominal pain



Counseling Points: GLP-1 RA & GLP-1/GIP

- Avoid if personal or family history of medullary thyroid cancer
- Start at lower dose and titrate
- Eat smaller *nourishing* meals to reduce nausea
- Avoid high fat meals -
- Reconsider nausea as feeling full
- Store extra pens in fridge
- Avoid in combo with DPP-4 inhibitors
- Report any sudden abdominal pain or pancreatitis symptoms
- Ask about recent eye exam
  - Potential increase in diabetes retinopathy

If on Metformin and Sulfonylurea – A1c 8.4 - Struggling with weight

- 44-year-old on Metformin and Sulfonylurea, A1c 8.4. Struggling with weight, BMI 36.
  Possible next options?

  Refer to RD / RDN

  Suggest tirzepatide (Mounjaro) if covered by insurance.
  If not, once weekly GLP-1 RA

Incretin Mimetics – How do they rate?

Question	Answer
Cause hypoglycemia?	No
Cause weight gain?	No
Affordable?	No
Lowers CV risk?	Yes*
Can most tolerate /use?	Yes/No (GI)

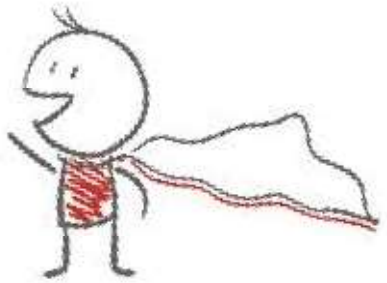
What questions for JR?

- JR is 72 yrs old, BMI 27, lives alone, A1c 7.3%. History of stroke. DM for 12 yrs, “diet controlled”. GFR is 42, UACR is 89 mg/g. Most meds covered by insurance.

Poll Question 6 – answer later

72 yr old, BMI 27, lives alone, A1c 7.3. History of stroke. “Diet controlled”. GFR is 42, UACR is 89 mg/g. Most meds covered by insurance.

- What is best next action?



a. Start Metformin

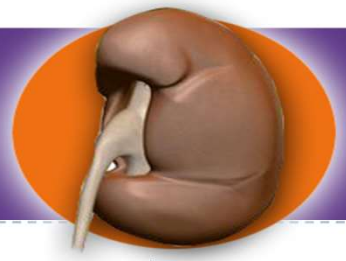
b. Consider SGLT-1 Inhibitor

c. Start low dose glipizide

d. Continue current strategy and ongoing monitoring

e. Consider DPP-IV Inhibitor (sitagliptin or linagliptin)

SGLT2 Inhibitors- "Glucoretics"



- **Action**: "Glucoretic" decreases renal reabsorption in the proximal tubule of the kidneys (reset renal threshold and increase glucosuria). Risk of ketoacidosis, Fournier's gangrene

Common Oral Diabetes Meds

Class/Main Action	Name(s)	Daily Dose Range	Considerations
SGLT2 Inhibitors "Glucoretic" • Decreases glucose reabsorption in kidneys	Canagliflozin* (Invokana)	100 - 300 mg 1x daily	**Side effects:** hypotension, UTIs, genital infections, increased urination, weight loss, ketoacidosis. **Heart Failure, CV & Kidney Protection:** 1st line therapy for Heart Failure (HF), Kidney Disease (CKD), Cardiovascular Disease, before or with metformin. **Considerations:** See Package Insert (PI) for GFR cut-offs, dosing. Limited BG lowering effect if GFR < 45, still benefits kidneys & heart at lower GFR. If CKD & GFR ≥20, use SGLT-2 to reduce CVD, HF, preserve renal function. (ADA/EASD) **Benefits:** SGLT-2s* reduce BG, CV death & HF, slow CKD. †Approved for peds, 10 yrs +. Lowers A1C 0.6% to 1.5%.
	Dapagliflozin* (Farxiga)	5 - 10 mg 1x daily	
	Empagliflozin*† (Jardiance)	10 - 25 mg 1x daily	
	Ertugliflozin (Steglatro)	5 – 15 mg 1x daily	
	Bexagliflozin (Brenzavvy)	20 mg 1x daily	

PocketCards updated annually. Download FREE CDCES Coach App for latest updates and notifications.

Benefits of SGLT-2 Inhibitors

A1C lowering

Weight loss

Cardiovascular benefits

Renal benefits

Heart failure benefits

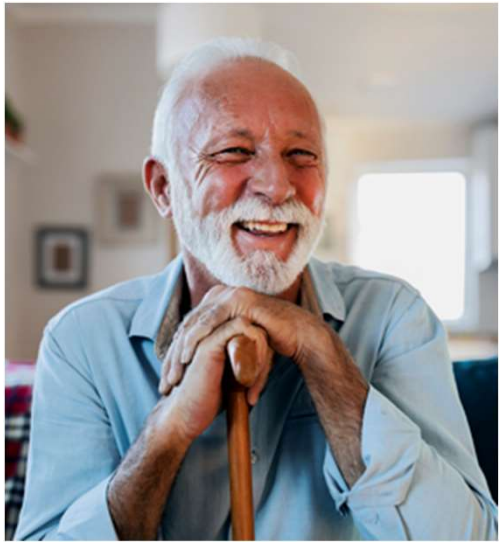
Blood pressure lowering

SGLT-2i Indications Summary

Drug	Lower BG	Reduce CV Risk?	Use to treat Heart Failure?	Slow renal disease?
Dapagliflozin (Farxiga)	Yes	Yes	Yes +/- Diabetes	Yes
Empagliflozin (Jardiance)	Yes	Yes	Yes +/- Diabetes	Yes
Canagliflozin (Invokana)	Yes	Yes	Yes w/ Diabetes	Yes
Ertugliflozin (Steglatro)	Yes		Yes w/ Diabetes	Yes
Bexagliflozin (Brenzavvy)	Yes		Yes w/Diabetes	Yes

SGLT2i: Managing Adverse Effects

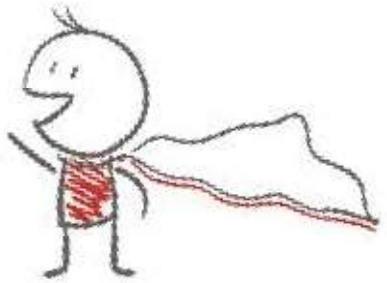
- Maintain good hygiene to reduce risk of genital mycotic infections
  - Higher risk with higher glucose
- DKA risk
  - Use caution with reducing insulin dose
- Monitor BP
  - May need to reduce antihypertensive meds
- UTI risk greater with hyperglycemia
- Amputations observed with canagliflozin
  - Good foot care, check feet daily
- Monitor renal function/potassium



Poll Question 6

72 yr old, BMI 27, lives alone, A1c 7.3. History of stroke. “Diet controlled”. GFR is 42, UACR is 89 mg/g. Most meds covered by insurance.

- What is best next action?



a. Start Metformin

b. Consider SGLT-1 Inhibitor

c. Start low dose glipizide

d. Continue current strategy and ongoing monitoring

e. Consider DPP-IV Inhibitor (sitagliptin or linagliptin)

SGLT2 Inhibitors- How do they rate?

Question	Answer
Cause hypoglycemia?	No
Cause weight gain?	No
Affordable?	No
Lowers HF risk?	Yes
Lowers CKD risk?	Yes
Lowers CV Risk?	Yes*

DPP-4 Inhibitors – "Incretin Enhancers"

Januvia (sitagliptin) – Tradjenta (linagliptin) Nesina (alogliptin)

- **Action:**
  - Increase insulin release w/ meals
  - Suppress glucagon
- **Efficacy:** Decreases A1c by 0.6 -0.8%
- Alogliptin increased risk of heart failure
- AWP $600 month

DPP – 4 Inhibitors "Incretin Enhancers" • Prolongs action of gut hormones • Increases insulin secretion • Delays gastric emptying	sitagliptin (Januvia)	25 - 100 mg daily – eliminated via kidney*	*If creat elevated, see med insert for dosing. **Side effects:** headache and flu-like symptoms. **Can cause severe, disabling joint pain.** Contact MD, stop med. Report signs of pancreatitis. †Alogliptin can increase risk of heart failure. Notify MD for shortness of breath, edema, weakness, etc. No wt gain or hypoglycemia. Lowers A1c 0.6%-0.8%.
	linagliptin (Tradjenta)	5 mg daily – eliminated via feces	
	alogliptin (Nesina)†	6.25 - 25 mg daily – eliminated via kidney*	

DPP-IV Inhibitors – How do they rate?

Question	Answer
Cause hypoglycemia?	No
Cause weight gain?	No
Affordable?	No
Lowers CV risk?	No
Can most tolerate /use?	Yes

Other Oral Diabetes Medications

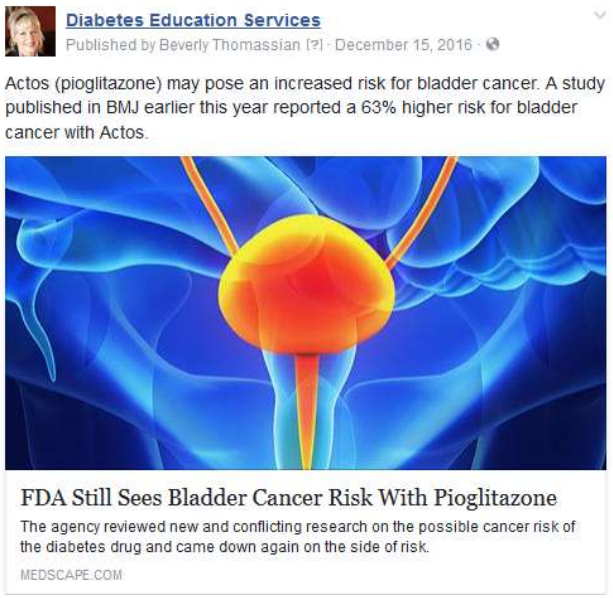
PocketCards updated annually. Download FREE CDCES Coach App for latest updates and notifications.

Class/Main Action	Name(s)	Daily Dose Range	Considerations
Thiazolidinediones "TZDs" • Increases insulin sensitivity	pioglitazone (Actos) rosiglitazone (Avandia)	15 – 45 mg daily 4 – 8 mg daily	Black Box Warning: TZDs may cause or worsen CHF. Monitor for edema and weight gain. Increased peripheral fracture risk. Actos may increase risk of bladder cancer. Lowers A1c 0.5% – 1.0%
Glucosidase Inhibitors • Delays carb absorption	acarbose (Precose) miglitol (Glyset)	25 – 100 mg w/meals; 300 mg max daily dose	Start low dose, increase at 4-8 wk intervals to decrease GI effects. Caution with liver or kidney problems. In case of hypo, treat w/ glucose tabs. Lowers A1c 0.5– 1.0%.
Meglitinides • Stimulates rapid insulin burst	repaglinide (Prandin)	0.5 – 4 mg w/meals (metabolized in liver)	Take before meals. Side effects may include hypoglycemia and weight gain. Lowers A1c 1.0% – 2.0%.
	nateglinide (Starlix)	60 – 120 mg w/meals (eliminated via kidney)	
Dopamine Receptor Agonists • Resets circadian rhythm	bromocriptine mesylate—Quick Release "QR" (Cycloset)	1.6 to 4.8 mg a day (each tab 0.8 mg)	Take within 2 hrs of waking. Side effects: nausea, headache, fatigue, hypotension, syncope, somnolence. Lowers A1c 0.6% – 0.9%.
Bile Acid Sequestrants • Decreases cholesterol / BG levels.	Colesevelam HCL (Welchol)	Up to six (6) 625 mg pills (3 tabs am, 3 tabs pm) 3.75gm packet in 4-8 ounces of fluid	Do not use if history of bowel obstruction, triglycerides >500, or pancreatitis. Can decrease absorption of certain meds, soluble vitamins. Lowers LDL by 15-30%. Side effects GI in nature. Lowers A1c 0.5%

Indications for Insulin Sensitizers

Rosiglitazone (Avandia), Pioglitazone (Actos)

- **Action**: decrease insulin resistance by making muscle and adipose cells more sensitive to insulin. Decrease free fatty acids



- **Names**:
  - pioglitazone (Actos) – bladder cancer warning
  - Indicated for steatosis liver disease
  - Post stroke
    - Dosing: 15-45 mg daily (try lower doses)
  - rosiglitazone (Avandia) – restriction relaxed
    - Dosing: 4-8 mg daily (rarely used)
- **Efficacy/ Considerations**
  - Reduce A1C ~0.5-1.0%
  - 6 weeks for maximum effect
  - Actos $5 a month, Avandia $330 a month
  - Can cause fluid retention, not indicated w/ CHF

Combo Oral Medications PocketCard™

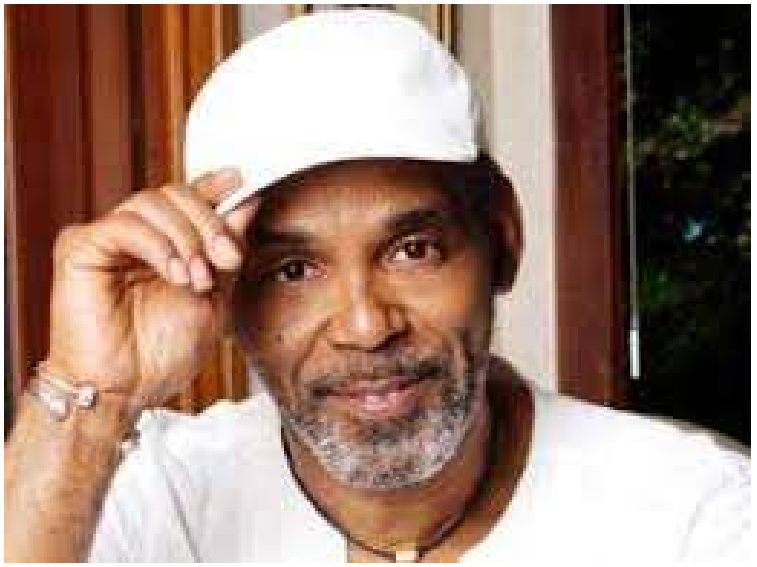
PocketCards updated twice a year. Download FREE CDCES Coach App for latest updates and notifications.

Medications	Doses in mg	Medications	Doses in mg	Medications	Doses in mg
Trijardy XR (3 meds) empagliflozin linagliptin metformin XR	 5 - 25 2.5 -5 1000	Janumet (sitagliptin/ metformin)	50/500 50/1000	Prandimet (repaglinide/ metformin)	1/500 2/500
ACTOplus Met* (pioglitazone/ metformin)	15/500 15/850	Janumet XR (sitagliptin/ metformin)	50/500 50/1000 or 100/1000	Qtern (saxagliptin / dapagliflozin)	5/10
ACTOplus Met XR (pioglitazone/ metformin	15/1000 30/1000	Jentadueto (linagliptin/ metformin)	2.5/500 2.5/850 or 2.5/1000	Segluromet (ertugliflozin/ metformin)	2.5/500 or 2.5/1000 or 7.5/500 or 7.5/1000
Duetact* (pioglitazone/ glimepiride)	30/2 30/4	Kazano (alogliptin/ metformin)	12.5/500 12.5/1000	Steglujan (ertugliflozin/ sitagliptin)	5/100 or 15/100
Glucovance* (glyburide/ metformin)	1.25/250 2.5/500 5/500	Metaglip* (glipizide/ metformin)	2.5/250 2.5/500 or 5/500	Synjardy (empagliflozin/ metformin)	5/500 or 12.5/500 5/1000 or 12.5/1000
Glyxambi (empagliflozin and linagliptin)	10/5 25/5	Oseni (alogliptin/ pioglitazone)	12.5/15 or 25/15 12.5/30 or 25/30 12.5/45 or 25/45	Synjardy XR† (empagliflozin/ metformin XR)	5/1000 or 10/1000 12.5/1000, 25/1000 †Approved for peds
Invokamet (canagliflozin/ metformin)	50/500 or 50/1000 150/500 or 150/1000	Diabetes Education SERVICES 25 years		Xigduo XR (dapagliflozin/ metformin)	5/500 or 10/500 5/1000 or 10/1000

***Available in generic. Observe precautions of each component drug.**

What next?

- 65 year old male, BMI 25, on Metformin 1000mg BID and Exenatide 10mcg before breakfast and dinner. History of a heart failure.
- A1c 8.9%. GFR 63, UACR 37mg/g.



Poll Question 7

- What next? 65 yrs, BMI 25, on max dose Metformin/Exenatide. History of heart failure. A1c 8.9%. GFR 63, UACR 37mg/g.

  a. Add a once weekly GLP-1 RA.

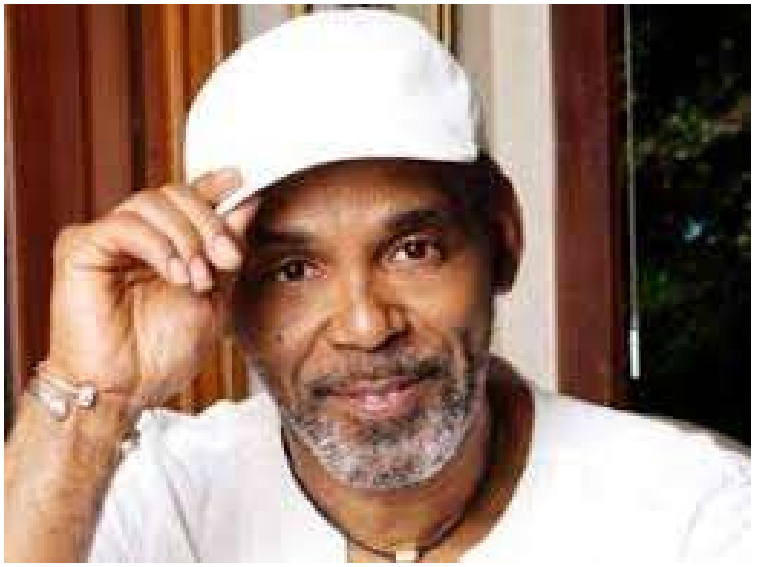
  b. Start basal insulin

  c. Add SGLT-2 Inhibitor

  d. Start bolus insulin

What questions?

- 67-year-old male, BMI 25, weighs 90kg. Takes Metformin 1000mg BID, Bydureon 2mg once weekly and empagliflozin (Jardiance 25mg).
- A1c 9.5%. GFR 63, UACR 37mg/g.
- Provider wants to start insulin. How much?



Intensifying Injectable Therapy – Type 2

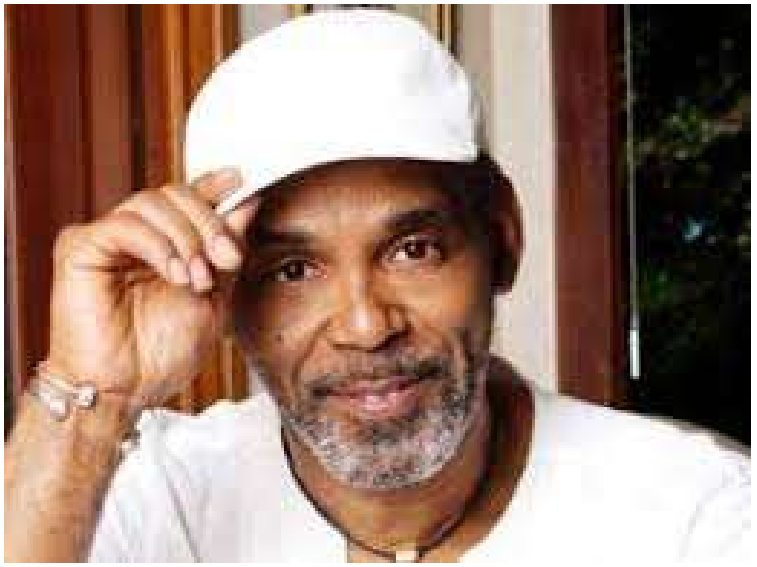
- Consider GLP-1 RA first
- Start basal insulin 10 units or 0.1 to 0.2 units/kg day
- Titrate up 2 units every 3 days, until FBG at goal
- If AM hypo, decrease basal insulin 20%
- Over basalization if basal >0.5 unit/kg day, add bolus insulin
- Adding bolus
  - Start with 4 units bolus at largest meal or
  - Start 1-2 injections with 10% of basal or
  - Switch to basal bolus combo (like 70/30 ins)

American Diabetes Association Diabetes Care 2023

If A1C 10%, insulin or sulfonylurea is indicated.

What questions?

- 67-year-old male, BMI 25, weighs 90kg. Takes Metformin 1000mg BID, Bydureon 2mg once weekly and empagliflozin (Jardiance 25mg).
- A1c 9.5%. GFR 63, UACR 37mg/g.
- Starts with 10units glargine (Basaglar).



Insulin/Injectable Combos

PocketCards updated annually. Download FREE CDCES Coach App for latest updates and notifications.

Name	Combines	Considerations
iDegLira* Xultophy 100/3.6	Insulin degludec (IDeg or Tresiba) Ultra long insulin + Liraglutide (Victoza) GLP-1 Receptor Agonist (GLP-1 RA)	**Xultophy 100/3.6 pre-filled pen** = 100 units IDeg / 3.6 mg liraglutide per mL Once daily injection – Dose range 10 to 50 = 10 – 50 units IDeg + 0.36 -1.8 mg liraglutide **Recommended starting dose:** • 16 IDegLira (= 16 units IDeg + 0.58 mg liraglutide) Titrate dose up or down by 2 units every 3-4 days to reach target. Supplied in package of five single-use 3mL pens. Once opened, good for 21 days.
iGlarLixi* Soliqua 100/33	Insulin glargine (Lantus) Basal Insulin + Lixisenatide (Adlyxin) GLP-1 Receptor Agonist	**Soliqua 100/33 Solostar Pen** = 100 units glargine / 33 µg lixisenatide per mL Once daily injection an hour prior to first meal of day. Dose range 15 – 60 = 15-60 units glargine + 5 – 20µg lixisenatide **Recommended starting dose:** • 15 units if not meeting glucose target on 30 units basal insulin or GLP-1 RA • 30 units if not meeting glucose target on 30-60 units basal insulin or GLP-1 RA Titrate dose up or down by 2-4 units every week to reach target. Supplied in package of five single-use 3mL pens. Once opened, good for 14 days.

*Discontinue basal insulin /GLP-1 RA therapy before starting. If dose missed, resume with next usual scheduled dose.

Critical Points

- Individualize Glycemic targets & BG-lowering approaches.
- 1st-line med based on careful assessment.
- MNT, exercise, & education: foundation T2DM therapy.
- ASCVD, Heart failure and CKD risk reduction - a major focus of therapy.
- Most important, all treatment decisions should be made in conjunction with the person's preferences, needs & values.
- Diabetes advocates can break the cycle of clinical inertia and improve well being.

Thank You

- Questions? Bryanna is here to help.
- Email info@diabetesed.net
- 530-893-8635
- Chat – DiabetesEd.net

Diabetes Education SERVICES