



# Pharmacologic Management of Type 2 Diabetes in Persons Living with HIV-Non Insulin Therapies: It's a Slam Dunk!

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# Abbreviations

- Type 2 diabetes (T2DM)
- American Diabetes Association (ADA)
- American Association of Clinical Endocrinologists (AACE)
- Hemoglobin A1c (HbA1c)
- Antiretroviral (ARV) Therapy
- Protease inhibitors (PI)
- Blood glucose (BG)
- Fasting plasma glucose (FPG)
- Fasting blood glucose (FBG)
- Postprandial blood glucose (PPG)
- Sulfonylureas (SU)
- Thiazolidinediones (TZDs)
- Dipeptidyl peptidase 4 inhibitors (DPP4-i)

# Abbreviations

- Sodium glucose cotransporter 2 inhibitors (SGLT2i)
- Glucagon-like peptide 1 receptor agonists (GLP1 RA)
- Meglitinides (Glinides)
- Alpha glucosidase inhibitors (AGi)
- Total daily dose (TDD)
- Contraindication (CI)
- Black box warning (BBW)
- Atherosclerotic cardiovascular disease (ASCVD)
- Heart failure (HF)
- Chronic kidney disease (CKD)

# Objectives

- Identify antihyperglycemic therapy used in the treatment of individuals with T2DM and HIV
- Design a treatment plan for individuals with T2DM and HIV
- Monitor antihyperglycemic therapy based on laboratory parameters and/or clinical presentation while accounting for drug interactions
- Identify counseling pearls for antihyperglycemic therapies

# ADA 2019 Treatment Algorithm

## Initiation of Therapy

- Metformin monotherapy

## Dual Therapy

- Consider if not at goal after 3 months of monotherapy or if HbA1c is  $\geq 1.5\%$  from their goal
- **Consider ASCVD, CKD, and HF benefits**
- **Cost/hypoglycemia/weight gain should be considered in those without ASCVD, CKD, or HF**

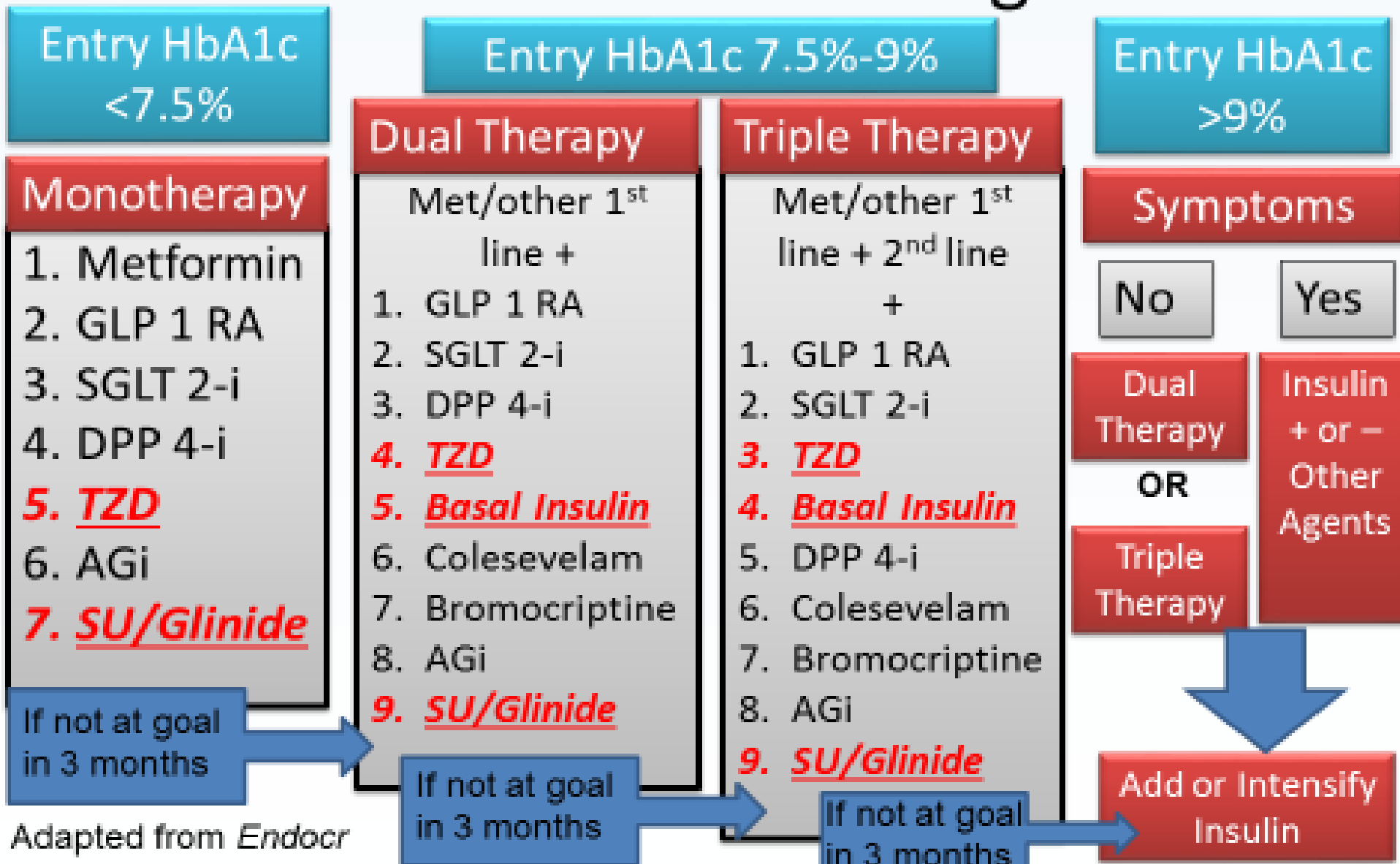
## Triple Therapy

- Consider if not at goal after 3 months of dual therapy
- **Consider ASCVD, CKD, HF cost, hypoglycemia, and weight gain**

## Combination Injectable Therapy

- Consider if not at goal after 3 months of triple therapy
- Consider insulin if HbA1c is  $\geq 10\%$  or BG is  $>300$  mg/dl at diagnosis
- **Consider ASCVD, CKD, HF cost, hypoglycemia, and weight gain**

# AACE 2018 Treatment Algorithm



Adapted from *Endocr Pract.* 2018;24(1):91-120

**Red italics underlined: Use Caution**

# Metformin Considerations

- GI counseling points
- Heart failure consideration
- Vitamin B12 deficiency-periodic monitoring
- May improve lipoaccumulation (mixed evidence) but may worsen lipoatrophy
- CI: Renal insufficiency
  - Lactic acidosis (SOB, weakness, dizziness, muscle pain)
    - Dolutegravir (Tivicay®) controversy
      - Consideration not to exceed 1000 mg daily of metformin?
    - Bictegravir, emtracitabine, tenofovir (Biktarvy®)
      - May increase serum concentrations of metformin
    - *Stavudine (d4t) and didanosine (ddi) interaction*



# Metformin Renal Impairment

- Initiation of metformin
  - GFR:  $>45$  mL/min/1.73m<sup>2</sup>
- Continuation of metformin:
  - GFR:  $>30$  mL/min/1.73m<sup>2</sup>
  - *Consider dose adjustment if GFR: 30-45 mL/min/1.73m<sup>2</sup>*
- Discontinue metformin in nausea/vomiting, or dehydration





# GLP 1 RA

- Exenatide extended release (Bydureon®)
  - 2 mg subq **once weekly**
- Liraglutide (Victoza®)
  - Initial: 0.6 mg subq **once daily** for 1 week
  - Titrate to 1.2 mg subq once daily for maintenance
  - Maximum 1.8 mg subq once daily
- Lixisenatide (Adlyxin®)
  - Initial: 10 mcg sub q **once daily** for 14 days
  - Titrate to 20 mcg subq once daily for maintenance

# GLP 1 RA

- Albiglutide (Tanzeum®)
  - Initial: 30 mg subq **once weekly**
  - Titrate to 50 mg subq once weekly if needed
- Dulaglutide (Trulicity®)
  - 0.75 mg subq **once weekly**
  - May increase to 1.5 mg subq once weekly if needed
- Semaglutide (Ozempic®)
  - 0.25 mg **once weekly** subq for 4 weeks then increase to 0.5 mg once weekly maintenance
  - Increase to 1 mg if necessary



# SGLT2-i

- Canagliflozin (Invokana®) 100-300 mg before first main meal
- Dapagliflozin (Farxiga®) 5-10 mg daily in AM
- Empagliflozin (Jardiance®) 10-25 mg daily in AM
- Ertugliflozin (Steglatro®) 5-15 mg daily in AM
- Monitor renal function



# SGLT2-i ADEs

- BBW: canagliflozin may increase risk of leg and foot amputations
- GU infection, polyuria, dehydration, hypotension, dizziness, increased LDL, bone fractures (canagliflozin)
- Rare: DKA
- Ritonavir can increase clearance of canagliflozin
  - May need to increase canagliflozin dose to 300 mg

# DPP4-i Medications

Medication	Dose	Renal Adjustment
Sitagliptin (Januvia®)	100 mg PO daily	CrCl 30-49 ml/min: 50 mg PO daily CrCl <30 ml/min or dialysis: 25 mg PO daily
Saxagliptin (Onglyza®)	2.5-5 mg PO daily	CrCl $\leq$ 50 ml/min or hemodialysis: 2.5 mg PO daily Do not exceed 2.5 mg daily if on strong CYP 3A4/5 inhibitors (such as ritonavir)
Linagliptin (Tradjenta®)	5 mg PO daily	No renal adjustment
Alogliptin (Nesina®)	25 mg PO daily	CrCl 30-59 ml/min: 12.5 mg PO daily CrCl <30 ml/min or hemodialysis: 6.25 mg PO daily

- Is there a correlation with DPP4i and reduction in CD4 count?

# SU

Medication	Usual dosage
Glipizide (Glucotrol®)	5-40 mg (TDD) (above 15 mg, initiate BID dosing)
Glipizide XL (Glucotrol XL®)	5-20 mg (TDD) once daily
Glyburide (Diabeta®)	1.25-20 mg (TDD) (above 10 mg, dose BID)
Glimepiride (Amaryl®)	1-8 mg (TDD) (indicated once daily; however, will sometimes be divided with larger doses)

# TZDs

Drug	Initial Dose	Max
Pioglitazone (Actos®)	15-30 mg daily	30-45 mg/day
Rosiglitazone (Avandia®)	4 mg daily	8 mg/day (may be divided in two doses)

# Other Non-insulin Therapy Considerations

## Sulfonylureas

- Renal considerations
  - Glipizide preferred
- Adverse effects
  - Weight gain
  - Hypoglycemia

## Thiazolidinediones

- Levels of TZDs can increase in combination with CYP2C8 inhibitors (many PIs)
- Hepatic considerations
- Adverse effects
  - Weight gain
  - Fluid retention (HF concern)



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# Combination Therapy Considerations

- Each additional agent added to initial therapy will lower HbA1c by approximately 0.7-1%
- ASCVD, CKD, and/or HF
- Cost
- Adverse effects

**ASCVD or CKD + metformin & lifestyle**

**ASCVD  
Predominates**

**GLP1 RA  
(liraglutide or  
semaglutide)  
and/or  
SGLT2i  
(empagliflozin or  
canagliflozin)**

**If not at goal  
(utilize GLP 1 RA  
or SGLT2 i)**

- DPP-4i\*\*
- Basal Insulin (degludec)
- Low Dose TZD
- SU

**HF or CKD  
Predominates**

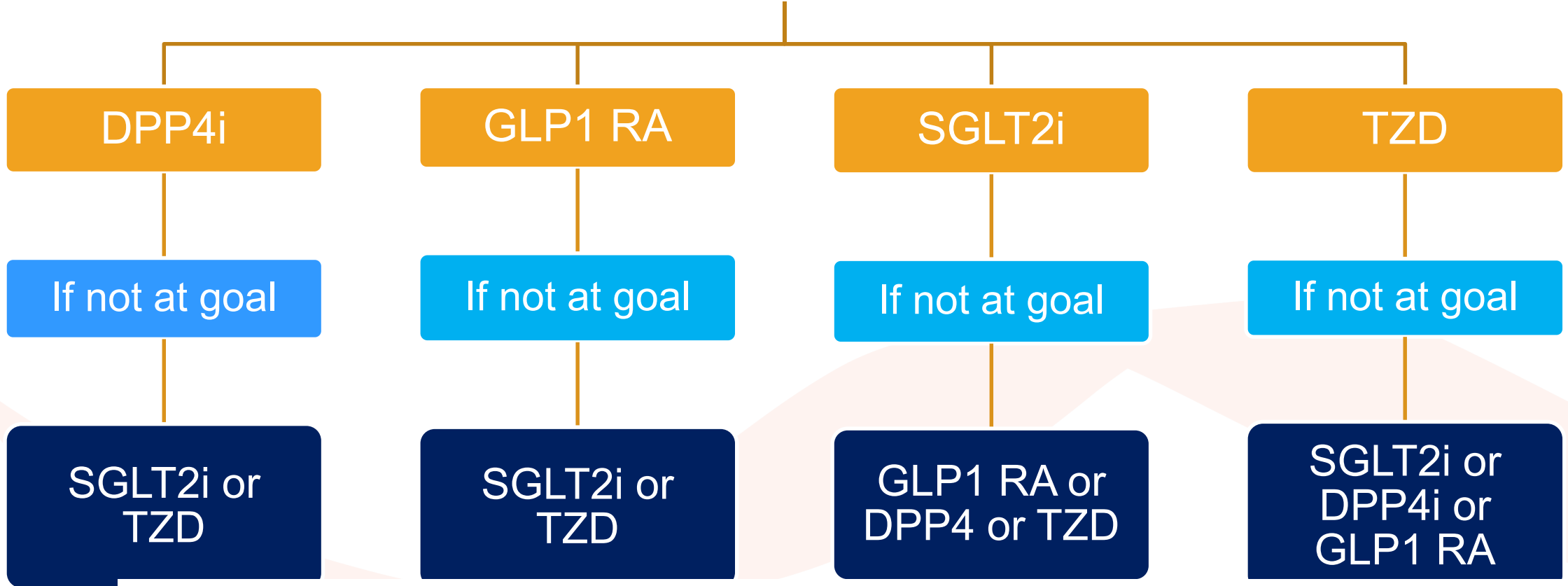
**SGLT2i First Line  
(empagliflozin or  
canagliflozin)  
or  
GLP 1 RA  
(liraglutide or  
semaglutide)**

**If not at goal  
(utilize GLP 1 RA)**

- DPP4i\*\* (avoid saxagliptin in HF)
- Basal Insulin (degludec)
- SU

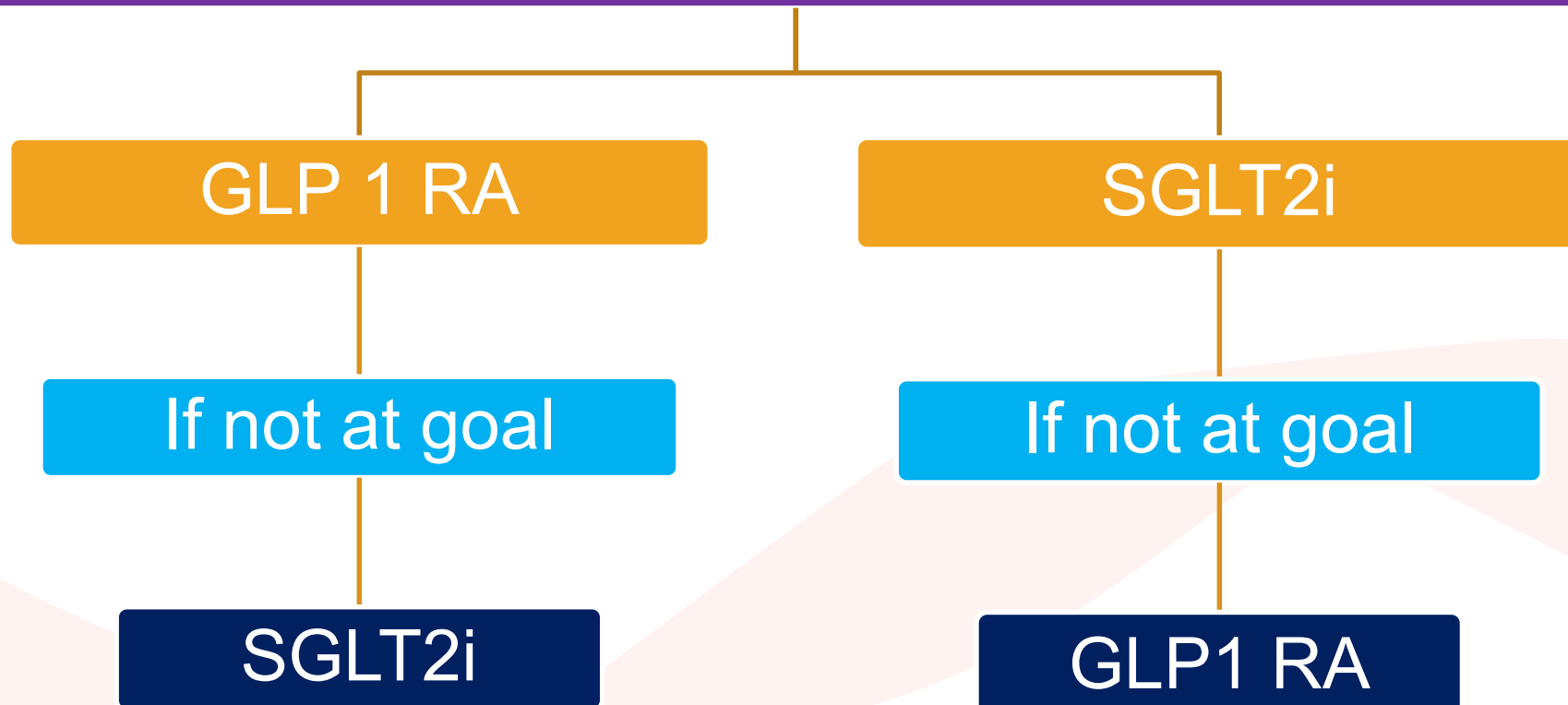
**\*\*Do not combine DPP4i and GLP1 RA**

**Minimize Hypoglycemia**  
*without established ASCVD, CKD, or HF*  
(+ metformin & lifestyle)



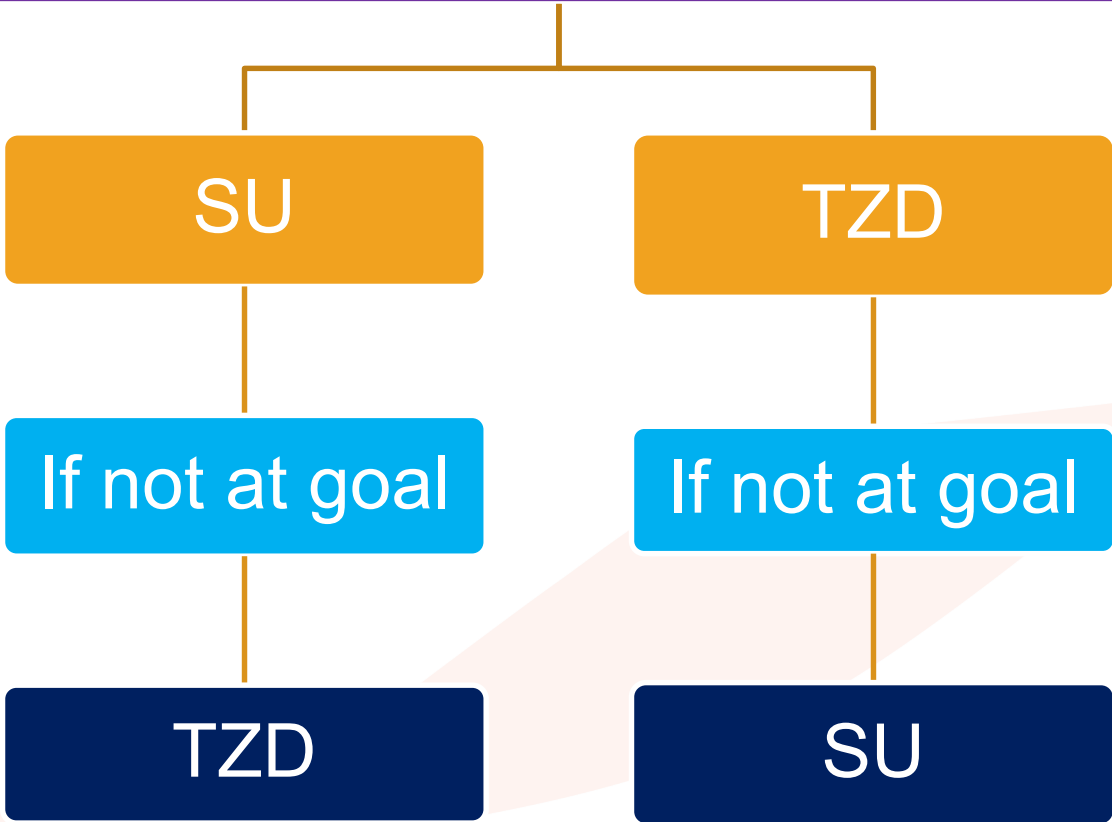
- If not at goal, can continue with additional agents as shown above
- If above agents have been utilized, consider SU or basal insulin
- **\*\*Do not combine DPP4i and GLP1 RA**

**Minimize Weight Gain/Promote Weight Loss  
*without established ASCVD, CKD, or HF*  
(+ metformin & lifestyle)**



- **If not at goal, or cannot tolerate the above agents, consider a DPP4i if not currently on a GLP1 RA**
- **Use caution with SU, TZD, Basal insulin**

**Minimize Cost**  
*without established ASCVD, CKD, or HF*  
(+ metformin & lifestyle)



**If above agents have been utilized, consider basal insulin, DPP4i OR SGLT2i with lowest cost**

# Case 1:

- MG is a 43 YOF who presents to clinic with a PMH of T2DM and HIV
- Her current medications include: metformin 500 mg BID and Symtuza once daily
- Pertinent labs include:
- HbA1c: 7.5%
- What would you recommend?
  - Medication, labs, monitoring
  - Does the patient have ASCVD? HF? CKD?
  - Is cost an issue? Weight gain?

140	101	19	160
3.8	20	0.8	

# How would you Proceed with MG?

- Increase metformin to optimal dosing and reassess
- Discontinue metformin since it is not working
- Increase metformin to 1000 mg twice daily and consider an add-on agent
- No change necessary since MJ is currently at goal



# Case 2

- LR is a 63 YOM who presents to clinic with a PMH of T2DM, HIV, and MI (2006, 2016)
- Her current medications include: metformin 1000 mg BID, Toprol XL 50 mg daily, and Symtuza once daily
- Pertinent labs include: 

140	101	19	150
4.4	20	0.8	
- HbA1c: 7.8%
- What would you recommend?

# How would you proceed for LR

- Addition of liraglutide once daily
- Addition of glipizide once daily
- Addition of pioglitazone once daily
- Addition of saxagliptin once daily

**ASCVD or CKD + metformin & lifestyle**

**ASCVD  
Predominates**

**GLP1 RA  
(liraglutide or  
semaglutide)  
and/or  
SGLT2i  
(empagliflozin or  
canagliflozin)**

**If not at goal  
(utilize GLP 1 RA  
or SGLT2 i)**

**DPP-4i\*\***

**Basal Insulin  
(degludec)**

**Low Dose TZD**

**SU**

**HF or CKD  
Predominates**

**SGLT2i First Line  
(empagliflozin or  
canagliflozin)  
or  
GLP 1 RA  
(liraglutide or  
semaglutide)**

**If not at goal  
(utilize GLP 1 RA)**

**DPP4i\*\* (avoid  
saxagliptin in HF)**

**Basal Insulin  
(degludec)**

**SU**

**\*\*Do not combine DPP4i and GLP1 RA**

# Summary

- Consider patient related factors in decision making
- Utilize drug information resources to identify drug interactions

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