



# Diabetes and Oral Medications

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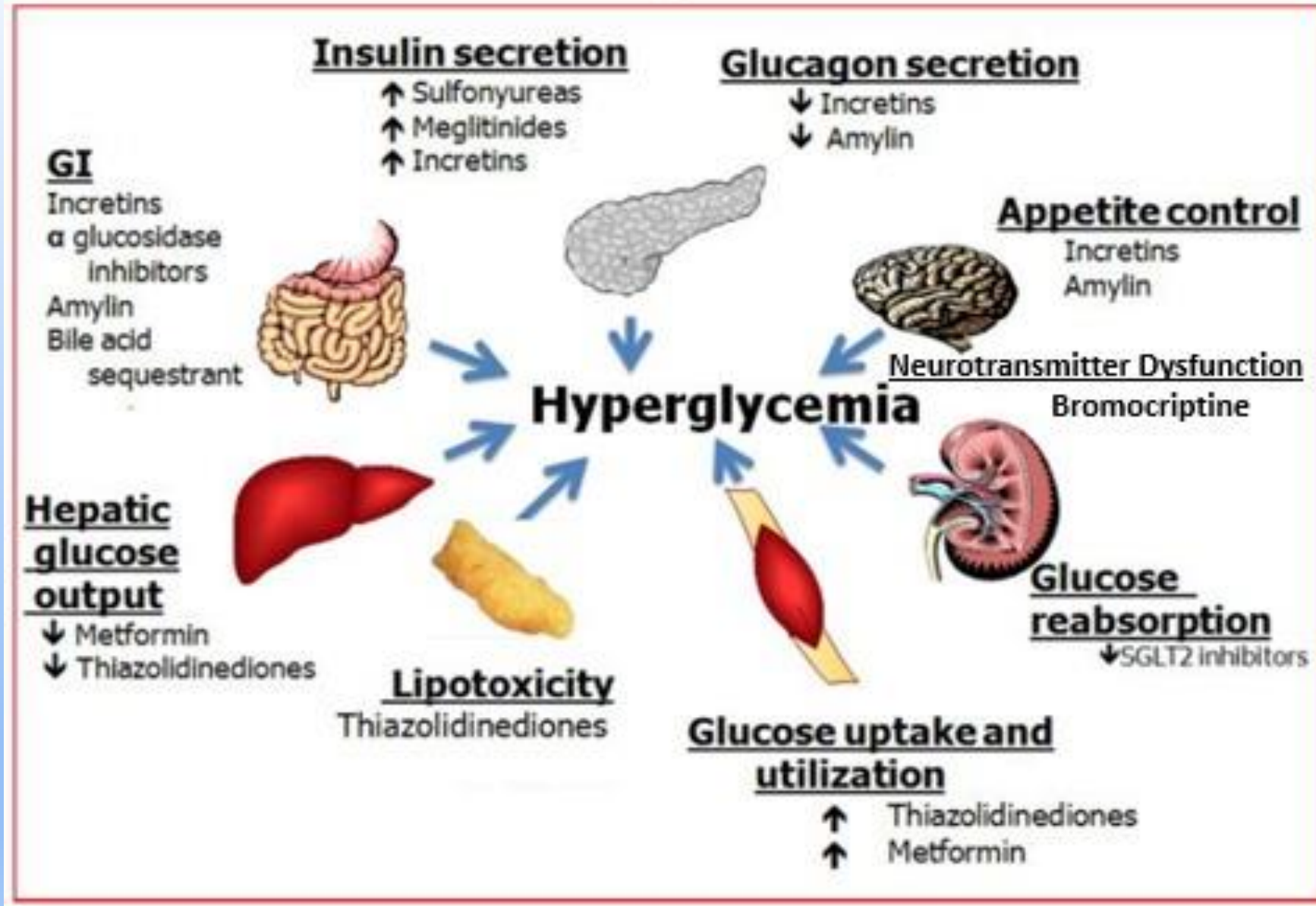
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# Objectives

- Identify common oral medications for diabetes
- Understand the role of oral medication in diabetes management
- Recognize side effects and patient responses to oral medications for diabetes management



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# Metformin

Mechanism of action: inhibits glucose production and absorption; increases insulin sensitivity in muscle and fat

Initial dose: 500 mg twice daily or 850 mg once daily (immediate release); 500 mg once daily (extended release)

Max dose: 2,000 to 2,550 mg divided twice to three times daily (immediate release); 2,000 mg once to twice daily (extended release)

A1c reduction: 1%

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# Metformin

- Advantages:
  - Weight neutral to modest weight loss
  - Helps decrease insulin gain
  - No hypoglycemia risk
  - Cost
- Disadvantages:
  - Adverse effects: diarrhea, nausea
  - Potential for lactic acidosis
- In many combination products

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# Sodium-glucose co-transporter 2 (SGLT2) inhibitors

Mechanism of action: blocks glucose and sodium reabsorption in the kidney; increases urinary excretion of glucose, sodium, and uric acid; and decreases plasma volume

A1c reduction: 0.5 to 0.7%

# Sodium-glucose co-transporter 2 (SGLT2) inhibitors

| Drug                       | Initial Dose      | Maximum Dose      |
|----------------------------|-------------------|-------------------|
| Bexagliflozin (Brenzavvy®) | 20 mg once daily  | 20 mg once daily  |
| Canagliflozin (Invokana®)  | 100 mg once daily | 300 mg once daily |
| Dapagliflozin (Farxiga®)   | 5 mg once daily   | 10 mg once daily  |
| Empagliflozin (Jardiance®) | 10 mg once daily  | 25 mg once daily  |
| Ertugliflozin (Steglatro®) | 5 mg once daily   | 15 mg once daily  |

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# Sodium-glucose co-transporter 2 (SGLT2) inhibitors

- Advantages:
  - Weight loss: 2-3 kg
  - No hypoglycemia risk
  - Additional benefits:
    - Cardiovascular Effects: MACE—benefit with canagliflozin and empagliflozin
    - Heart Failure—dapagliflozin (10 mg) and empagliflozin (10 mg) are indication for treatment; benefit with canagliflozin and ertugliflozin but no indication for heart failure alone
    - Chronic Kidney Disease—dapagliflozin (10 mg) and empagliflozin (10 mg) are indicated for treatment of CKD; canagliflozin shown benefit with delaying progression of diabetic kidney disease although not indicated for CKD

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# Sodium-glucose co-transporter 2 (SGLT2) inhibitors

- Disadvantages:
  - Adverse effects: genital yeast infections, UTI
  - Rare adverse effects: ketoacidosis, volume depletion, acute pancreatitis, fracture risk (conflicting evidence), Fournier's gangrene
  - Cost

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## Sulfonylureas-Second Generation

Mechanism of  
action: stimulate  
pancreatic  
insulin secretion

A1c reduction:  
0.6 to 1.2%

# Sulfonylureas-Second Generation

| Drug                   | Initial Dose                                     | Maximum Dose                      |
|------------------------|--------------------------------------------------|-----------------------------------|
| Glimepiride            | 1 to 2 mg once daily (1 mg in kidney impairment) | 8 mg once daily                   |
| Glipizide IR           | 5 mg once daily                                  | 20 mg twice daily                 |
| Glipizide XL           | 5 mg once daily                                  | 20 mg once daily                  |
| Glyburide (standard)   | 2.5 to 5 mg once daily                           | 10 mg twice daily                 |
| Glyburide (micronized) | 1 to 3 mg once daily                             | 12 mg once or divided twice daily |

# Sulfonylureas-Second Generation

## Advantages:

- Cost

## Disadvantages:

- Weight gain: glyburide more weight gain than glipizide and glimepiride
- Hypoglycemia risk: greatest risk with glyburide; least risk with glipizide
- Avoid glyburide in kidney impairment
- Short-lived efficacy

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# Dipeptidyl peptidase-4 (DPP-4) inhibitors

- Mechanism of action: increase insulin secretion in response to elevated blood glucose, decreases glucagon secretion, and slows gastric emptying; reduces postprandial glucose
- A1c reduction: 0.5 to 0.7%

# Dipeptidyl peptidase-4 (DPP-4) inhibitors

| Drug        | Dose                   |
|-------------|------------------------|
| Alogliptin  | 25 mg once daily       |
| Linagliptin | 5 mg once daily        |
| Saxagliptin | 2.5 to 5 mg once daily |
| Sitagliptin | 100 mg once daily      |

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# Dipeptidyl peptidase-4 (DPP-4) inhibitors

## Advantages:

- No hypoglycemia risk
- Potentially cost—alogliptin and saxagliptin generic

## Disadvantages:

- Risk of new or worsening heart failure with saxagliptin and alogliptin
- Rare adverse effects: severe joint pain, pancreatitis, bullous pemphigoid

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# Pioglitazone

- Mechanism of action: increases insulin sensitivity in liver, muscle, and fat
- Initial dose: 15 to 30 mg once daily
- Maximum dose: 45 mg once daily
- A1c reduction: 0.7 to 0.9%

# Pioglitazone

## Advantages:

- No hypoglycemia risk
- Cost
- Reduces triglycerides
- Sustains glycemic control over diabetes course better than metformin or sulfonylureas

## Disadvantages:

- Weight gain
- Serious adverse effects: edema, heart failure, fractures
- Do not use in bladder cancer; caution with history of bladder cancer

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# Alpha-Glucosidase Inhibitors

- Mechanism of action: slows intestinal carbohydrate digestion/absorption to reduce postprandial glucose
- A1c reduction: 0.7 to 0.8% (acarbose); ~0.3 to 0.8% (miglitol monotherapy)
- Acarbose and miglitol:
  - Initial: 25 mg once daily to three times daily (with meals)
  - Maximum: 300 mg divided three times daily (with meals)

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# Alpha-Glucosidase Inhibitors

- Advantages:
  - No hypoglycemia risk
- Disadvantages:
  - GI side effects (e.g. abdominal pain, flatulence, diarrhea)

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# Meglitinides

- Mechanism of action: stimulates pancreatic insulin secretion
- A1c reduction: 0.7 to 1.1%
- Drugs:
  - Nateglinide: 180 to 360 mg, divided three times daily with meals
  - Repaglinide: initial 1 to 2 mg with meals (0.5 mg if A1c < 8%); maximum 16 mg divided four times daily
- Taken within 30 minutes before meal; skip dose if skipping meal

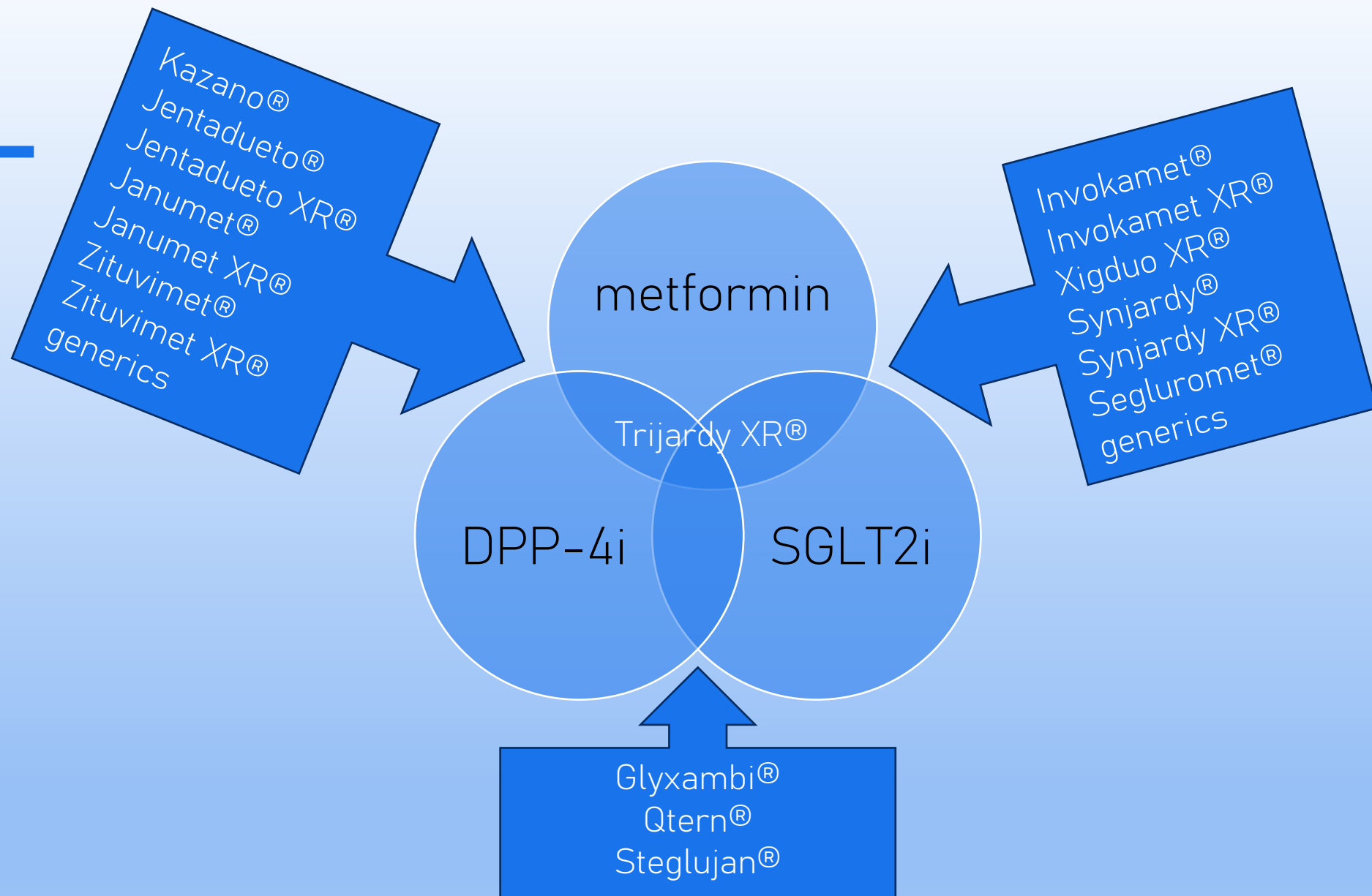
# Meglitinides

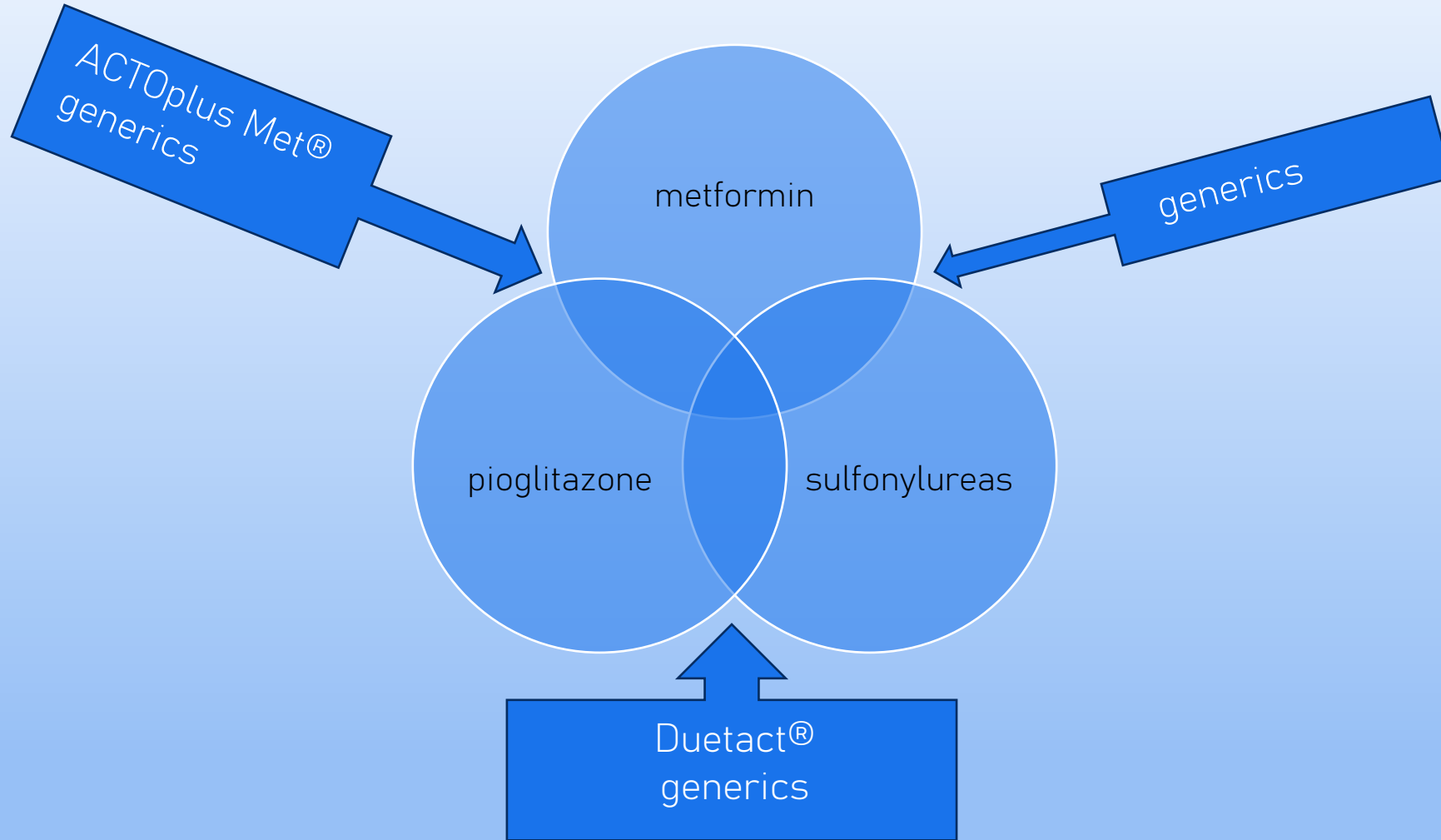
## Advantages:

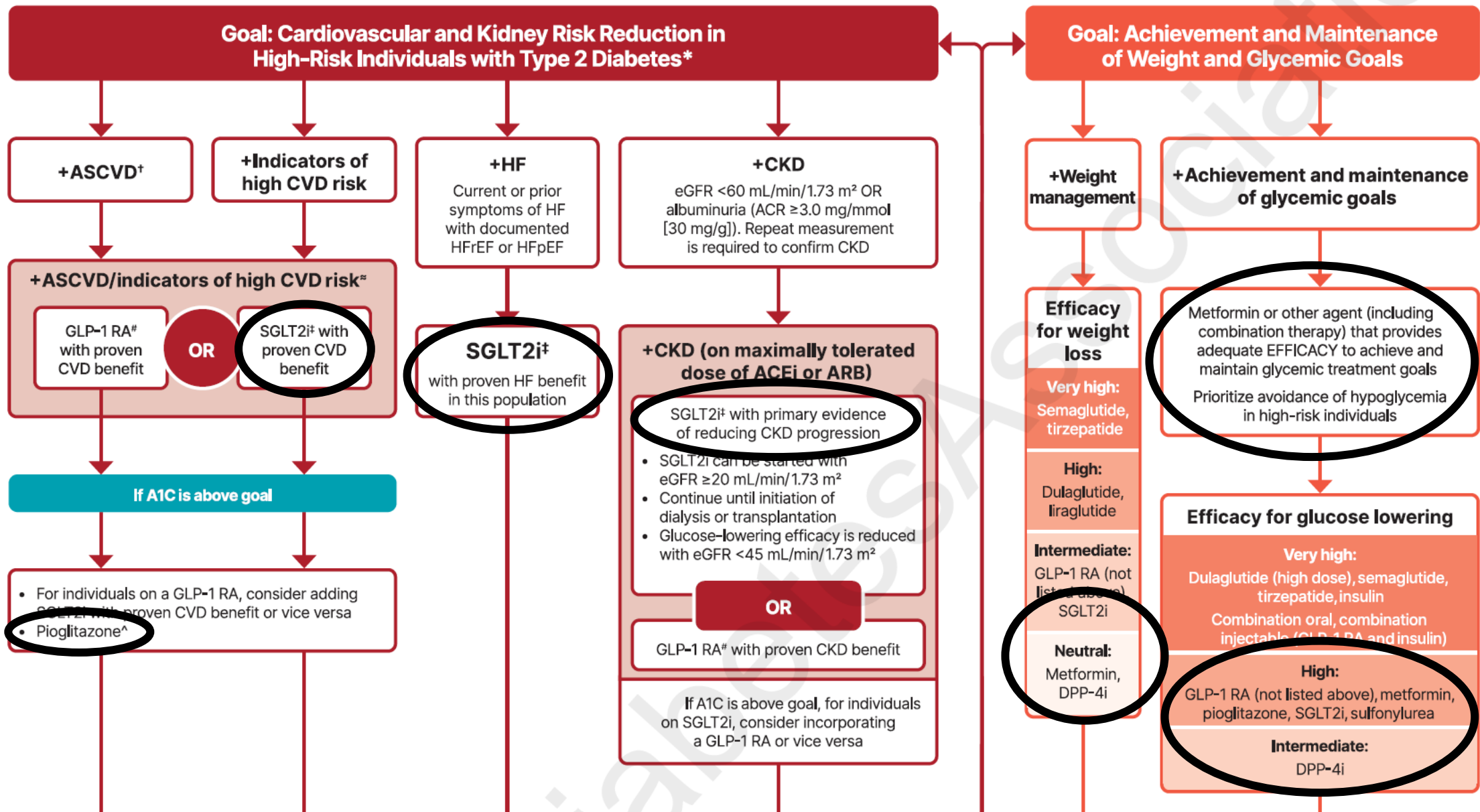
- Reduces postprandial glucose more than sulfonylureas
- Safer than sulfonylureas in kidney impairment

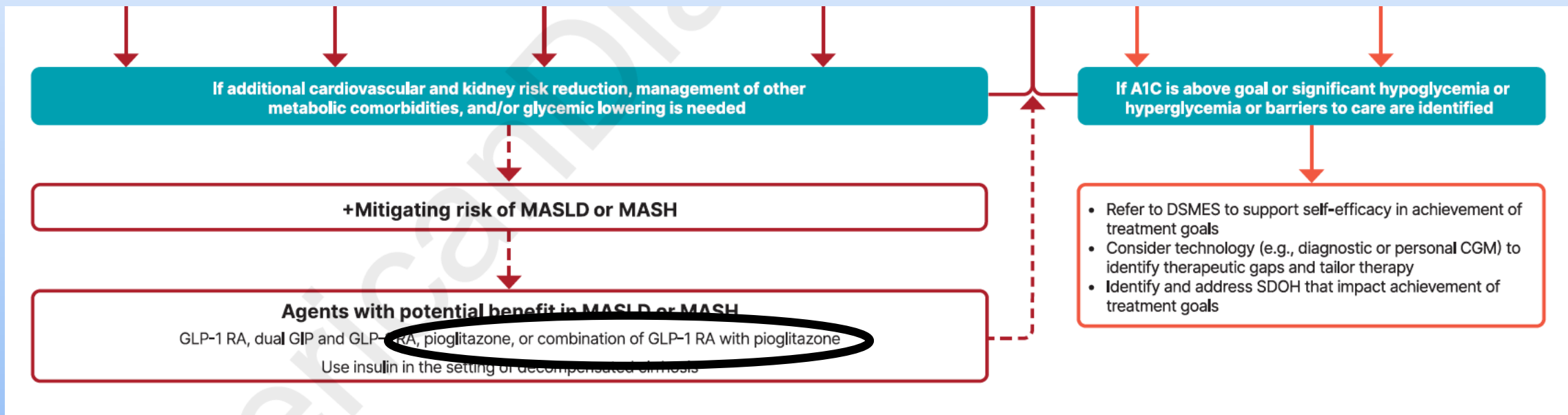
## Disadvantages:

- Weight gain
- Hypoglycemia risk (less than sulfonylureas)









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# References

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# Questions

