NCLEX-RN · 2026 TEST PLAN · HIGH-YIELD PHARMACOLOGY

Oral Antidiabetics

The 8 major classes used to manage Type 2 Diabetes Mellitus (T2DM)

System: Endocrine | Target: Blood Glucose & HbA1c | Framework: NCJMM Clinical Judgment | Priority: Hypoglycemia Safety

QUICK INDEX

1 Drug Overview

WHY WE GIVE IT

- **Primary indication:** Type 2 Diabetes Mellitus (T2DM) — when diet, exercise, and lifestyle modifications fail to achieve glycemic targets.
- **NOT for Type 1 DM** — Type 1 requires insulin (no functioning beta cells to stimulate). Exception: SGLT2 and metformin are occasionally used as adjuncts in T1DM in adults, but **NCLEX answer = insulin only for T1DM**.
- **Goal HbA1c:** generally < 7% (individualized — tighter for younger patients, looser for elderly/frail).
- **Goal fasting glucose:** 80–130 mg/dL. Goal postprandial (2-hr): < 180 mg/dL.
- **First-line: Metformin** (biguanide) is first-line for nearly all T2DM patients unless contraindicated.
- **Combination therapy** is common — different classes target different pathogenic defects (insulin resistance, insulin deficiency, glucagon excess, renal glucose reabsorption, incretin deficiency).

2 Mechanism of Action

SIMPLIFIED PATHWAYS BY CLASS

Biguanides (Metformin) → ↓ hepatic gluconeogenesis → ↑ peripheral insulin sensitivity → ↓ glucose absorption in gut

Sulfonylureas / Meglitinides → close K^+ channels on pancreatic β-cells → depolarization → ↑ **insulin release**

Thiazolidinediones (TZDs) → activate PPAR-γ receptor → ↑ insulin sensitivity in muscle & adipose tissue

DPP-4 Inhibitors ("-gliptins") → block DPP-4 enzyme → ↑ incretin (GLP-1) → ↑ insulin / ↓ glucagon (glucose-dependent)

SGLT2 Inhibitors ("-gliflozins") → block glucose reabsorption in proximal tubule → **glucose excreted in urine**

Alpha-glucosidase inhibitors → block intestinal enzyme → ↓ carbohydrate breakdown → ↓ postprandial glucose spike

GLP-1 agonists (oral semaglutide) → mimic incretin → ↑ insulin, ↓ glucagon, delay gastric emptying, ↑ satiety

3 Therapeutic Effects

HOW YOU KNOW IT'S WORKING

GLYCEMIC MARKERS

- HbA1c ↓ toward < 7%
- Fasting glucose 80–130 mg/dL
- Postprandial < 180 mg/dL
- No symptoms of hyper- or hypoglycemia

CLINICAL IMPROVEMENT

- Resolution of polyuria, polydipsia, polyphagia (the "3 Ps")
- Stable weight (weight loss with SGLT2, GLP-1, metformin)
- Improved energy, wound healing
- No DKA / HHS episodes

SECONDARY BENEFITS (CLASS-SPECIFIC)

- **SGLT2:** ↓ CV mortality, ↓ HF hospitalizations, renal protection
- **GLP-1:** ↓ CV events, weight loss
- **Metformin:** modest weight loss, no hypoglycemia alone

4 Side Effects & Adverse Reactions

COMMON VS LIFE-THREATENING

COMMON (BOTHERSOME)

- **Metformin:** GI upset, diarrhea, metallic taste, B12 deficiency (long-term)
- **Sulfonylureas:** weight gain, hypoglycemia, photosensitivity
- **TZDs:** weight gain, peripheral edema, fluid retention
- **DPP-4:** headache, nasopharyngitis, arthralgia
- **SGLT2:** genital mycotic infections (yeast), UTIs, polyuria, volume depletion
- **Alpha-glucosidase:** flatulence, abdominal cramping, diarrhea
- **GLP-1 (oral sema):** nausea, vomiting, early satiety

SERIOUS / LIFE-THREATENING

- **Metformin → LACTIC ACIDOSIS** (black box): muscle pain, malaise, respiratory distress, hypotension, hypothermia
- **Sulfonylureas / Meglitinides → severe HYPOGLYCEMIA** (can be prolonged in elderly, renal failure)
- **TZDs → HF exacerbation, MI, bladder cancer (pioglitazone), hepatotoxicity, fractures**
- **DPP-4 → acute pancreatitis, severe joint pain, bullous pemphigoid, HF (saxagliptin)**
- **SGLT2 → EUGLYCEMIC DKA** (normal glucose + ketoacidosis), Fournier's gangrene, AKI, lower limb amputation (canagliflozin)
- **GLP-1 → pancreatitis, thyroid C-cell tumors (black box), gastroparesis**

Toxicity pearls: Metformin lactic acidosis → serum lactate > 5, anion gap acidosis, pH < 7.35. SGLT2 euglycemic DKA can occur with glucose < 200 mg/dL — do NOT rule out DKA based on normal glucose.

5 Priority Nursing Considerations

ASSESS · MONITOR · HOLD · NOTIFY

- → **ASSESS** blood glucose before administration; ask about last meal and hypoglycemia symptoms.
- → **MONITOR** renal function (BUN, creatinine, **eGFR**) — critical for metformin and SGLT2.
- → **MONITOR** liver function (ALT, AST) for TZDs and sulfonylureas.
- → **HOLD METFORMIN** 24–48 hours *before* and 48 hours *after* IV iodinated contrast dye. Restart only after renal function confirmed normal.
- → **HOLD SGLT2** at least 3 days before scheduled surgery (ertugliflozin: 4 days) to prevent euglycemic DKA.
- → **HOLD sulfonylureas** if patient is NPO, acutely ill, or eating poorly — risk of hypoglycemia.
- → **NOTIFY PROVIDER** for: muscle pain + malaise (lactic acidosis), abdominal pain radiating to back (pancreatitis), worsening edema/SOB/weight gain (HF), genital/perineal pain with fever (Fournier's gangrene).

⚠ **Contraindications at a glance:**

- **Metformin:** eGFR < 30, active liver disease, heart failure with hypoxia, severe infection/sepsis, chronic alcohol use, contrast imaging
- **Sulfonylureas:** sulfa allergy (cross-sensitivity), T1DM, DKA, severe renal/hepatic impairment
- **TZDs:** NYHA Class III/IV heart failure (black box), active liver disease, bladder cancer history
- **SGLT2:** eGFR < 30 (varies), recurrent UTI/yeast infections, DKA history, T1DM

Drug interactions: Sulfonylureas + beta-blockers = masked hypoglycemia symptoms (no tachycardia — only diaphoresis shows). Metformin + alcohol = ↑ lactic acidosis risk. SGLT2 + loop diuretics = volume depletion. TZDs + insulin = ↑ HF risk.

6 Labs & Diagnostics

NUMBERS YOU MUST KNOW

GLYCEMIC LABS

- **HbA1c:** goal < 7% (every 3 mo)
- **FBG:** 80–130 mg/dL
- **2-hr PPG:** < 180 mg/dL
- **Hypoglycemia:** < 70 mg/dL (treat!)

RENAL FUNCTION

- **Creatinine:** 0.6–1.3 mg/dL
- **eGFR:** > 60 normal; < 30 = stop metformin & most SGLT2
- **BUN:** 7–20 mg/dL
- Recheck q3–6 mo on metformin/SGLT2

LIVER & OTHER

- **ALT/AST:** < 40 U/L; stop TZD if > 3× upper limit
- **Lactate:** < 2 mmol/L (> 5 = severe lactic acidosis)
- **B12:** check yearly on metformin
- **Urine ketones / β-hydroxybutyrate:** any SGLT2 patient with unexplained symptoms

🚨 **Critical values to report immediately:** Glucose < 50 or > 400 mg/dL · Lactate > 5 · Creatinine ↑ 50% from baseline · ALT/AST > 3× normal · K^+ < 3.0 or > 6.0

7 Administration & Safety

ROUTE · TIMING · SPECIAL INSTRUCTIONS

- **Metformin:** PO with meals (reduces GI upset). Extended-release: once daily with dinner — **do NOT crush or chew**. Titrate slowly.
- **Sulfonylureas (glipizide, glyburide, glimepiride):** PO 30 minutes *before* breakfast. **Patient MUST eat** or hypoglycemia will occur.
- **Meglitinides (repaglinide, nateglinide):** PO 15–30 minutes before meals; skip dose if skipping meal ("no meal = no pill").
- **TZDs (pioglitazone, rosiglitazone):** PO once daily with or without food. Takes 2–12 weeks for full effect.
- **DPP-4 ("-gliptins"):** PO once daily, with or without food.
- **SGLT2 ("-gliflozins"):** PO once daily in the morning (polyuria at bedtime disrupts sleep). Encourage hydration.
- **Alpha-glucosidase (acarbose, miglitol):** PO with *first bite* of each meal.
- **Oral semaglutide (Rybelsus):** PO on empty stomach, with ≤ 4 oz water, ≥ 30 min before first food/drink/other meds.

⚠ **High-alert safety:** Oral antidiabetics are NOT on the ISMP "high-alert" list like insulin, but sulfonylureas in elderly are a leading cause of drug-induced hypoglycemic hospitalizations. Double-check dosing in patients > 65 or with CKD.

8 Patient Education

WHAT THEY MUST KNOW BEFORE DISCHARGE

- **Recognize hypoglycemia:** shakiness, sweating, confusion, hunger, palpitations, dizziness. Treat immediately with 15 g fast-acting carb (4 oz juice, 3 glucose tabs, regular soda) → recheck in 15 min → repeat if still < 70.
- **Acarbose / miglitol exception:** Treat hypoglycemia with **PURE GLUCOSE (glucose tablets or gel) — NOT table sugar, juice, or candy.** These drugs block sucrose breakdown!
- **Sick-day rules:** Continue oral antidiabetics if able to eat/drink. **HOLD metformin and SGLT2** if dehydrated, vomiting, acutely ill, or febrile — risk of lactic acidosis or euglycemic DKA.
- **Alcohol:** Avoid or strictly limit — ↑ hypoglycemia risk (sulfonylureas) and ↑ lactic acidosis risk (metformin).
- **Wear medical ID** identifying diabetes and medications.
- **Carry glucose source** at all times.
- **SGLT2 patients:** maintain hydration; report perineal pain/swelling/fever immediately (Fournier's gangrene).
- **Seek emergency care for:** severe abdominal pain, muscle pain with weakness, chest pain/SOB, confusion, persistent vomiting, fruity breath.

9 NCLEX Test Traps

⚠ WHAT STUDENTS GET WRONG

- **Trap #1 — Acarbose + table sugar:** Sucrose WON'T raise blood glucose because alpha-glucosidase is blocked. **Correct answer: glucose tablets/gel.**
- **Trap #2 — Metformin + contrast:** Must be held 24–48 hrs before AND 48 hrs after IV contrast. The question usually hides this in a CT scan or cardiac cath scenario.
- **Trap #3 — Sulfonylurea + beta-blocker:** Beta-blockers mask tachycardia. **Diaphoresis is the ONLY reliable hypoglycemia sign.**
- **Trap #4 — Euglycemic DKA on SGLT2:** Glucose of 180 does NOT rule out DKA. Check ketones / anion gap / pH.
- **Trap #5 — TZDs + heart failure:** Crackles, ↑ weight, SOB, peripheral edema = HOLD drug, notify. NOT just "a side effect — keep giving."
- **Trap #6 — "Skip dose if skipping meal":** Applies to meglitinides (repaglinide/nateglinide) — NOT metformin or long-acting agents.
- **Trap #7 — Hypoglycemia priority:** Conscious patient → 15 g oral carb. Unconscious → **IV dextrose 50% (D50)** or IM glucagon. Never give oral anything to an unconscious patient (aspiration risk).
- **Trap #8 — Metformin is NOT a secretagogue:** It doesn't cause hypoglycemia alone. If the question says "hypoglycemia," suspect sulfonylureas/meglitinides/insulin combo.
- **Trap #9 — Sulfa allergy:** Contraindicates sulfonylureas (possible cross-reaction).
- **Trap #10 — Priority action ≠ first thought:** If patient on metformin presents with muscle pain + SOB + hypotension → **lactic acidosis.** First action: assess ABCs and notify provider, do NOT give next metformin dose.

10 Memory Boosters

MNEMONICS & PATTERNS

SUFFIX RECOGNITION

- **"-formin"** → biguanide (metformin)
- **"-ide / -zide"** → sulfonylurea (glipizide, glyburide, glimepiride)
- **"-glinide"** → meglitinide (repaglinide)
- **"-glitazone"** → TZD (pioglitazone)
- **"-gliptin"** → DPP-4 (sitagliptin)
- **"-gliflozin"** → SGLT2 (empagliflozin)
- **"-glutide"** → GLP-1 (semaglutide)

"LACTIC" — METFORMIN HOLD CRITERIA

- **L**iver disease
- **A**lcohol abuse
- **C**ontrast dye
- **T**issue hypoxia (HF, sepsis)
- **I**nfection / severe illness
- **C**reatinine high / eGFR < 30

"COLD & CLAMMY → NEED SOME CANDY"

- Cold/clammy = hypoglycemia → give sugar
- Hot/dry = hyperglycemia → need insulin
- Works for all diabetic patients

RULE OF 15S (HYPOGLYCEMIA)

- **15 g** fast carb
- Wait **15 min**
- Recheck glucose
- Repeat up to **3×**, then notify provider

GLIFLOZINS = "PEE OUT SUGAR"

- Glucose in urine → yeast, UTI, polyuria
- Dehydration → hypotension, AKI
- Euglycemic DKA risk
- Think: "sweet urine = infection risk"

"NO MEAL = NO PILL"

- Applies to meglitinides + sulfonylureas
- Prevents hypoglycemia when NPO
- Teach before discharge

Most Tested Drugs in This Class

KEY DIFFERENCES · SIDE-BY-SIDE

Metformin (Glucophage)

Biguanide · FIRST-LINE for T2DM

MOA	↓ hepatic gluconeogenesis; ↑ insulin sensitivity
HYPO RISK	LOW (alone)
WEIGHT	Neutral / slight loss
BLACK BOX	Lactic acidosis
KEY HOLD	Contrast dye · eGFR < 30 · sepsis · HF decompensation
NCLEX PEARL	GI side effects improve after 2 wks; take with meals

Glipizide · Glyburide · Glimepiride

Sulfonylureas · 2nd-gen insulin secretagogues

MOA	Close β-cell K^+ channels → ↑ insulin release
HYPO RISK	HIGH (especially elderly)
WEIGHT	↑ weight gain
CONTRAINDIC.	Sulfa allergy · T1DM · severe renal/hepatic dx
KEY HOLD	NPO · skipping meals · acute illness
NCLEX PEARL	Give 30 min BEFORE breakfast — patient MUST eat

Repaglinide · Nateglinide

Meglitinides · rapid-acting secretagogues

MOA	Same as sulfonylureas but shorter duration
HYPO RISK	MODERATE
TIMING	15–30 min before each meal
GOLDEN RULE	**"No meal = No pill"**
USE CASE	Irregular eaters · post-prandial spikes
NCLEX PEARL	Shorter ½-life than sulfonylureas = safer in CKD

Oral Antidiabetics — NCLEX-RN High-Yield Infographic

Pioglitazone · Rosiglitazone

Thiazolidinediones (TZDs) · insulin sensitizers

MOA	Activate PPAR-γ → ↑ insulin sensitivity
HYPO RISK	LOW (alone)
BLACK BOX	HEART FAILURE · MI risk
WARNINGS	Bladder CA (pioglitazone), fractures (women), hepatotoxicity
KEY HOLD	NYHA Class III–IV HF · ALT > 3× normal
NCLEX PEARL	Monitor weight daily; report > 3 lb gain in 1 wk

Sitagliptin · Saxagliptin · Linagliptin

DPP-4 Inhibitors · incretin enhancers

MOA	Block DPP-4 → ↑ GLP-1 → glucose-dependent insulin
HYPO RISK	LOW
WEIGHT	Neutral
SERIOUS SE	Pancreatitis · severe arthralgia · bullous pemphigoid · HF (saxa)
CONTRAINDIC.	History of pancreatitis
NCLEX PEARL	Abdominal pain radiating to back = STOP + notify

Empagliflozin · Dapagliflozin · Canagliflozin

SGLT2 Inhibitors · "sugar in urine"

MOA	Block renal glucose reabsorption → glucosuria
HYPO RISK	LOW (alone)
BONUS BENEFITS	↓ CV mortality, ↓ HF hospitalizations, renal protection
SERIOUS SE	Euglycemic DKA · Fournier's gangrene · AKI · amputation (cana)
KEY HOLD	3 days before surgery · acute illness · dehydration
NCLEX PEARL	Check ketones if ill — normal glucose does NOT rule out DKA

Acarbose · Miglitol

Alpha-Glucosidase Inhibitors · "starch blockers"

MOA	Block intestinal carb breakdown → ↓ post-meal glucose
HYPO RISK	LOW (alone)
TIMING	With FIRST BITE of each meal
MAIN SE	Flatulence, diarrhea, abdominal cramping
TRAP	**Treat hypoglycemia with GLUCOSE TABLETS only — NOT sucrose/juice**
NCLEX PEARL	Classic NGN trap: "which snack treats hypoglycemia?" → glucose tabs

Oral Semaglutide (Rybelsus)

GLP-1 Receptor Agonist · oral incretin mimetic

MOA	Mimics GLP-1 → ↑ insulin, ↓ glucagon, delayed gastric emptying
HYPO RISK	LOW (alone)
WEIGHT	↓↓ Significant weight loss
BLACK BOX	Thyroid C-cell tumors (MTC)
TIMING	Empty stomach · ≤ 4 oz water · wait 30 min before food
NCLEX PEARL	Contraindicated in personal/family hx of MTC or MEN 2

FINAL SECTION — MANDATORY

Clinical Judgment Snapshot

#1 PRIORITY RISK

Hypoglycemia (sulfonylureas, meglitinides, combo therapy) and **lactic acidosis** (metformin) — both can kill within hours if unrecognized. On SGLT2: **euglycemic DKA**.

WHAT HARMS THE PATIENT FIRST

A patient taking a sulfonylurea who skips a meal will develop **neuroglycopenia** → confusion, seizure, coma — often within 2–4 hours. On metformin with sepsis/contrast: **lactic acidosis** → shock.

FIRST NURSING ACTION (SCENARIO)

Conscious + hypoglycemic: 15 g fast carb → recheck in 15 min. **Unconscious:** IV D50 or IM glucagon (NEVER PO). **Suspected lactic acidosis:** assess ABCs, hold metformin, notify provider, obtain lactate/ABG.

NCLEX-RN High-Yield Pharmacology · Oral Antidiabetics · Aligned to 2026 NCLEX Test Plan & NCJMM · For study purposes — always verify against current clinical guidelines and institutional protocols.