



ANTI-HISTAMINES

H1 & H2 Receptor Antagonists



System: Immune / Respiratory / GI



High-Alert Populations: Elderly, Children <2, BPH, Glaucoma



NCLEX 2026 Test Plan

1. DRUG OVERVIEW



Two Major Categories

- ▶ **H1 Blockers** → allergy, itching, motion sickness, sleep, anxiety, anaphylaxis adjunct
- ▶ **H2 Blockers** → GERD, peptic ulcer disease (PUD), stress ulcer prophylaxis, Zollinger-Ellison

Key Indications (Why We Give)

- ▶ Allergic rhinitis, urticaria (hives), pruritus, conjunctivitis
- ▶ Mild to moderate allergic reactions (**not** first-line for anaphylaxis — that's epinephrine)
- ▶ Motion sickness / vertigo (meclizine, dimenhydrinate)
- ▶ Insomnia / sedation (diphenhydramine, hydroxyzine)
- ▶ Anxiety (hydroxyzine — non-controlled, non-addictive)
- ▶ N/V prevention pre-op & post-op (promethazine, hydroxyzine)
- ▶ Extrapyramidal symptoms (EPS) from antipsychotics — diphenhydramine IV/IM
- ▶ H2 blockers → ↓ gastric acid for GERD, PUD, stress ulcer prevention

High-Yield Clinical Pearl: Antihistamines *do not* reverse bronchoconstriction in anaphylaxis. They are **adjunct only**. Epinephrine IM is the priority intervention.

2. MECHANISM OF ACTION



H1 Blockers

Allergen exposure → Mast cell degranulation → Histamine released
→ H1 receptors activated → **✗ BLOCKED by antihistamine**
→ ↓ Vasodilation ↓ Capillary permeability
→ ↓ Bronchoconstriction ↓ Itching ↓ Mucus secretion
→ Symptom relief **✓**

1st-Gen vs 2nd-Gen (Critical Distinction!)

- ▶ **1st-Gen (Diphenhydramine, Hydroxyzine, Promethazine):** Cross blood-brain barrier → CNS depression + strong anticholinergic effects
- ▶ **2nd-Gen (Loratadine, Cetirizine, Fexofenadine):** Do NOT cross BBB well → minimal sedation, minimal anticholinergic

H2 Blockers

Histamine normally binds H2 receptors on parietal cells → acid secretion
→ Drug **blocks H2 receptor** → ↓ HCl production
→ ↑ Gastric pH → Ulcer healing / GERD relief **✓**

3. THERAPEUTIC EFFECTS (What Says "It's Working")

- ▶ ↓ Sneezing, runny nose, itchy/watery eyes
- ▶ ↓ Hives, pruritus, rash resolution
- ▶ ↓ Nausea & vomiting (especially motion-related)
- ▶ ↓ Anxiety, improved sleep onset (hydroxyzine, diphenhydramine)
- ▶ Resolved EPS / dystonic reaction (diphenhydramine IV)
- ▶ **H2 blockers:** ↓ epigastric pain, ↓ heartburn, healed endoscopic ulcers, negative H. pylori retest (combo Tx)
- ▶ Clear breath sounds (as allergic component resolves — not a substitute for bronchodilator)

Objective wins to document: absence of urticaria, pruritus score improvement, decreased rhinorrhea, clearer sclera, patient report of restful sleep, decreased emesis episodes.

4. SIDE EFFECTS & ADVERSE REACTIONS

✓ COMMON (1st-Gen predominantly)

- ▶ Sedation, drowsiness, fatigue
- ▶ Dizziness, impaired coordination → **fall risk**
- ▶ Dry mouth, dry eyes, thickened secretions
- ▶ Blurred vision
- ▶ Constipation
- ▶ Urinary retention / hesitancy
- ▶ Tachycardia / palpitations
- ▶ Weight gain (cetirizine notably)
- ▶ **Paradoxical excitation** in children & elderly (agitation, hyperactivity)

🚨 SERIOUS & LIFE-THREATENING

- ▶ **Anticholinergic toxicity** → hyperthermia, delirium, seizures, coma (1st-gen overdose)
- ▶ **Seizures** (esp. diphenhydramine overdose — lowers seizure threshold)
- ▶ **QT prolongation & torsades de pointes** (high-dose diphenhydramine, hydroxyzine, promethazine)
- ▶ **Respiratory depression** (with opioids / alcohol / CNS depressants)
- ▶ **Promethazine IV extravasation** → severe tissue necrosis, gangrene, may require amputation (**BOXED WARNING**)
- ▶ **Promethazine in children <2 years** → fatal respiratory depression (**BOXED WARNING — CONTRAINDICATED**)
- ▶ **Neuroleptic Malignant Syndrome (NMS)** — rare, promethazine

- ▶ **Acute angle-closure glaucoma** attack (pupil dilation)
- ▶ **Acute urinary retention** in BPH → bladder rupture risk
- ▶ **Agranulocytosis, aplastic anemia** (rare; H2 blockers & promethazine)
- ▶ **Cimetidine**: gynecomastia, impotence, confusion (esp. elderly)

🚑 **TOXICITY TRIAD (1st-Gen OD)**: "Red as a beet, dry as a bone, hot as a hare, blind as a bat, mad as a hatter, full as a flask" → anticholinergic toxicity. **Antidote: Physostigmine** (use only in severe cases per poison control).

5. PRIORITY NURSING CONSIDERATIONS

ASSESS & MONITOR

- ▶ Baseline & ongoing: LOC, respiratory rate, BP, HR, O₂ sat
- ▶ Fall risk score (initiate fall precautions in elderly)
- ▶ Voiding pattern — watch for urinary retention (esp. BPH)
- ▶ Bowel pattern — assess for constipation
- ▶ Mental status — confusion, agitation, delirium (elderly = red flag)
- ▶ ECG in overdose or high-risk patients (QT interval)
- ▶ IV site q1-2h if promethazine infusing — **burning = STOP immediately**

HOLD THE DRUG IF...

- ▶ Severe respiratory depression / RR <12
- ▶ Altered LOC / excessive sedation
- ▶ Acute asthma exacerbation (thickens secretions — worsens)
- ▶ Urinary retention developing
- ▶ Signs of anticholinergic toxicity
- ▶ QTc prolongation on ECG
- ▶ IV promethazine: any patient report of burning/pain at site

CONTRAINDICATIONS

- ▶ **Children <2 years** (especially promethazine — fatal)
- ▶ **Narrow/closed-angle glaucoma**
- ▶ **BPH / bladder outlet obstruction**
- ▶ Severe asthma / acute asthma attack
- ▶ GI / GU obstruction
- ▶ MAOI use (current or within 14 days)
- ▶ Pregnancy/Lactation — weigh risk (loratadine & cetirizine preferred if needed)
- ▶ **Beers Criteria:** Avoid 1st-gen antihistamines in adults ≥ 65 (high anticholinergic burden → falls, delirium, dementia risk)

⚠ **DRUG INTERACTIONS**

- ▶ **CNS depressants** (opioids, benzos, alcohol, zolpidem) → additive sedation, respiratory depression
- ▶ **Other anticholinergics** (TCAs, oxybutynin, atropine) → additive toxicity
- ▶ **MAOIs** → hypertensive crisis, prolonged anticholinergic effects
- ▶ **QT-prolonging drugs** (ondansetron, azithromycin, haloperidol) → torsades risk
- ▶ **Cimetidine** = CYP450 inhibitor → ↑ levels of warfarin, phenytoin, theophylline, lidocaine, beta-blockers (famotidine preferred — fewer interactions)
- ▶ Grapefruit juice ↑ fexofenadine absorption issues (avoid)

📞 **NOTIFY PROVIDER**

- ▶ Seizure activity, syncope
- ▶ Chest pain, palpitations, new irregular rhythm
- ▶ Inability to void >6-8 hours
- ▶ Severe confusion/delirium in elderly

- ▶ IV promethazine extravasation — **emergency consult**

6. LABS & DIAGNOSTICS

- ▶ **CBC** — watch for agranulocytosis, aplastic anemia (rare, H2 blockers)
- ▶ **LFTs (ALT, AST)** — hepatic metabolism; caution in liver disease (most metabolized by CYP3A4)
- ▶ **BUN / Creatinine** — renal clearance; dose-adjust cetirizine, fexofenadine, H2 blockers in CKD
- ▶ **ECG / QTc** — baseline & with overdose or high-dose therapy
- ▶ **Serum electrolytes** — K^+ , Mg^{2+} (low levels ↑ torsades risk)
- ▶ **Bladder scan** — if suspected retention (>400 mL post-void = concerning)
- ▶ **H. pylori testing** — before long-term H2 blocker use for PUD (rule out infection)

Critical values to recognize: QTc > 500 ms (torsades risk), K^+ < 3.5, Mg^{2+} < 1.5, post-void residual > 400 mL.

7. ADMINISTRATION & SAFETY



Routes & Timing

- ▶ **PO:** most common — with or without food (food ↓ GI upset)
- ▶ **Fexofenadine:** take with water only — **no fruit juice** (↓ absorption up to 70%)
- ▶ **IM:** deep, large muscle (Z-track promethazine preferred)
- ▶ **IV:** slow push, dilute, large bore vein
- ▶ Meclizine: 1 hour before travel for motion sickness
- ▶ Sleep aids (diphenhydramine): 30 min before bed
- ▶ H2 blockers: with or without food; for GERD, at bedtime for nocturnal acid

HIGH-ALERT: IV PROMETHAZINE

- ▶ Preferred route is **deep IM** — IV is last resort
- ▶ Dilute to ≤25 mg/mL; infuse over 10-15 minutes
- ▶ Administer through large-bore, free-flowing IV in large vein (**avoid hand/wrist**)
- ▶ Stop IMMEDIATELY if patient reports burning/pain — extravasation causes necrosis/gangrene
- ▶ NEVER give SubQ or intra-arterial — can cause gangrene
- ▶ Contraindicated in children <2 years (fatal respiratory depression)

Special Populations

- ▶ **Elderly:** avoid 1st-gen (Beers); if needed, start low, go slow

- ▶ **Children:** NO diphenhydramine cough/cold products <4-6 yrs per FDA; NO promethazine <2 yrs
- ▶ **Pregnancy:** loratadine & cetirizine preferred; chlorpheniramine historically used
- ▶ **Hepatic/renal impairment:** dose adjustment required

8. PATIENT EDUCATION

- ▶ **No driving** or operating machinery until sedation effects known (1st-gen)
- ▶ **AVOID alcohol & CNS depressants** — additive sedation can be fatal
- ▶ Rise slowly from sitting/lying (orthostatic hypotension → falls)
- ▶ Sugar-free gum, ice chips, frequent oral care for dry mouth
- ▶ ↑ Fluids and fiber to prevent constipation
- ▶ Use sunscreen — photosensitivity possible
- ▶ Take fexofenadine with **water only** — no fruit juices (orange, apple, grapefruit)
- ▶ Don't crush/chew extended-release tablets
- ▶ Store out of reach of children (diphenhydramine OD is common accidental poisoning)
- ▶ Use as directed — do not double up if dose missed
- ▶ Tolerance to sedation may develop; tolerance to therapeutic effect may also occur (rotate or switch classes)

SEEK IMMEDIATE HELP IF: difficulty breathing, chest pain, fainting, seizure, unable to urinate >8 hrs, severe confusion, hallucinations, fast/irregular heartbeat, signs of allergic reaction (ironic — can occur), yellowing of skin/eyes.

9. NCLEX TEST TRAPS ⚠️



- ▶ **TRAP:** "Diphenhydramine for anaphylaxis" → ❌ Epinephrine IM is FIRST; diphenhydramine is adjunct only
- ▶ **TRAP:** Giving 1st-gen antihistamine to an elderly patient → Beers Criteria violation; expect confusion, falls, urinary retention
- ▶ **TRAP:** Giving promethazine to a 14-month-old → **NEVER** (fatal respiratory depression, boxed warning)
- ▶ **TRAP:** IV promethazine through a small hand vein → extravasation, gangrene risk. **Priority:** deep IM preferred; if IV, dilute & use large vein
- ▶ **TRAP:** Fexofenadine + orange juice → ↓ absorption. Teach **water only**.
- ▶ **TRAP:** BPH patient on diphenhydramine for sleep → acute urinary retention (anticholinergic)
- ▶ **TRAP:** Glaucoma patient on antihistamine → acute angle-closure attack (pupil dilation)
- ▶ **TRAP:** Antihistamine "relieves" asthma → ❌ thickens secretions, does NOT bronchodilate. Not a rescue drug.
- ▶ **TRAP:** Cimetidine for GERD in elderly → confusion, gynecomastia, numerous drug interactions. **Famotidine preferred.**
- ▶ **TRAP:** Non-sedating = no side effects → ❌ Still watch for QT prolongation, urinary retention, hepatic dosing
- ▶ **TRAP:** Paradoxical excitation in a child after diphenhydramine → this IS expected; don't mistake for allergic reaction
- ▶ **TRAP:** Teaching "take for 2 weeks to prevent allergies" → 2nd-gen antihistamines work best taken daily BEFORE exposure
- ▶ **PRIORITY ORDER:** Airway → Breathing → Circulation → Drug. If patient is in anaphylaxis: **EPI first**, then antihistamine + steroid as adjuncts.

10. MEMORY BOOSTERS

Anticholinergic "CAN'Ts" (1st-Gen Side Effects)

- ▶ Can't **SEE** — blurred vision, mydriasis
- ▶ Can't **PEE** — urinary retention
- ▶ Can't **SPIT** — dry mouth
- ▶ Can't **POOP** — constipation
- ▶ Can't **THINK** — confusion, delirium

Anticholinergic Toxicity (the Classic Six)

- ▶  **HOT** as a hare (hyperthermia)
- ▶  **RED** as a beet (flushing)
- ▶  **DRY** as a bone (anhidrosis)
- ▶  **BLIND** as a bat (mydriasis)
- ▶  **MAD** as a hatter (delirium)
- ▶  **FULL** as a flask (urinary retention)

Drug Class by Suffix Pattern

- ▶ H1 blockers often end in **-adine, -amine, -izine, -astine** (lor**ATADINE**, cetir**IZINE**, fexofen**ADINE**)

- ▶ H2 blockers end in **-tidine** (famoTIDINE, cimeTIDINE, ranITIDINE, nizaTIDINE)

"The 4 Z's" (2nd-Gen — non-sedating favorites)

- ▶ Zyrtec (cetirizine)
- ▶ Zizal / Xyzal (levocetirizine)
- ▶ Claritin & Clarinex (loratadine / desloratadine)
- ▶ Allegra (fexofenadine) — the **no-juice** one

Promethazine Safety — "P-R-O-M-E-T-H"

- ▶ **P**eds <2 = NO (fatal)
- ▶ **R**oute: IM preferred
- ▶ **O**bserve site (burning = STOP)
- ▶ **M**ost concentrated = most dangerous (dilute!)
- ▶ **E**xtravasation = gangrene
- ▶ **T**issue necrosis = emergency
- ▶ **H**and veins = AVOID

H1 vs H2 Quick Recall

- ▶ **H1** = "**H**ives, **H**ayfever, **H**eaves (vomit)"

▶ **H2** = "**H**earburn, **H**CL, **H**ealing ulcers"



CLINICAL JUDGMENT SNAPSHOT

**⚡ Q1: What is the #1 priority risk with antihistamines?**

Respiratory depression & CNS depression — especially with 1st-generation drugs combined with opioids, benzos, or alcohol. In children <2 with promethazine, this is *fatal*. In overdose, anticholinergic toxicity → seizures, arrhythmia, coma is the kill pathway.

⚡ Q2: What will harm the patient FIRST?

Airway compromise via over-sedation in the vulnerable patient (elderly, opioid-user, child).
Second-fastest: **extravasation injury** from IV promethazine — tissue necrosis within minutes.
In BPH patients: **acute urinary retention**. In glaucoma patients: **acute angle-closure attack**.

⚡ Q3: What is the FIRST nursing action in a scenario?

ANAPHYLAXIS: Give epinephrine IM FIRST → then secure airway → then antihistamine + steroid as adjuncts.

IV PROMETHAZINE + burning at site: STOP infusion immediately → disconnect tubing, leave catheter in place → aspirate any drug → notify provider → elevate extremity.

SUSPECTED OVERDOSE (diphenhydramine): Assess ABCs → monitor LOC + ECG → prepare for intubation if needed → notify provider + poison control → anticipate sodium bicarbonate (QRS widening), benzodiazepines (seizures), physostigmine only if severe.

ELDERLY with new confusion after diphenhydramine: Hold the drug → assess for urinary retention (bladder scan) → fall precautions → notify provider → advocate for switch to 2nd-gen or non-pharm sleep intervention.

⚡ Q4: Top NGN "Take Action" / "Evaluate" Decisions

- ✓ HOLD if: RR <12, SpO₂ <92%, unable to void, QTc >500, burning at IV site, acute asthma, <2 yrs old (promethazine).
- ✓ GIVE if: vitals stable, appropriate age/indication, patent large-bore IV, diluted, no contraindications.
- ✓ EVALUATE EFFECTIVENESS by: ↓ hives, ↓ pruritus, ↓ rhinorrhea, restful sleep, absence of N/V, healed ulcer on endoscopy (H2).

MOST-TESTED DRUGS IN THIS CLASS + KEY DIFFERENCES



Generic (Brand)	Gen / Type	Unique NCLEX Point
Diphenhydramine (Benadryl)	1st-Gen H1	Most sedating. Also IV for EPS/dystonia & anaphylaxis adjunct. OD = anticholinergic tox + seizures. Avoid in elderly (Beers).
Hydroxyzine (Vistaril / Atarax)	1st-Gen H1	Used for anxiety (non-controlled), pruritus, pre-op sedation. Monitor QT. Watch for dry mouth, sedation.
Promethazine (Phenergan)	1st-Gen H1	BOXED WARNING x2: fatal respiratory depression in <2 yrs; severe tissue necrosis with IV extravasation. Use deep IM; if IV, dilute + large vein.
Meclizine (Antivert, Bonine)	1st-Gen H1	Motion sickness & vertigo (Meniere's). Take 1 hr before travel. Less sedating than diphenhydramine.
Dimenhydrinate (Dramamine)	1st-Gen H1	Motion sickness. Very similar to diphenhydramine.
Chlorpheniramine	1st-Gen H1	Historically used in pregnancy for rhinitis. Less sedating than diphenhydramine but still 1st-gen.
Loratadine (Claritin)	2nd-Gen H1	Non-sedating. OTC. Daily allergy control. Safe in pregnancy (preferred).
Cetirizine (Zyrtec)	2nd-Gen H1	Mildly sedating (more than loratadine). Effective for chronic urticaria. Can cause weight gain.
Fexofenadine (Allegra)	2nd-Gen H1	NO fruit juice (↓ absorption up to 70%). Least sedating 2nd-gen. Take with water.

Generic (Brand)	Gen / Type	Unique NCLEX Point
Levocetirizine (Xyzal)	2nd-Gen H1	Isomer of cetirizine. Slightly more potent. Dose-adjust in renal impairment.
Desloratadine (Clarinex)	2nd-Gen H1	Active metabolite of loratadine. Rx only.
Famotidine (Pepcid)	H2 Blocker	Preferred H2. Few drug interactions. Renal dose adjustment needed.
Cimetidine (Tagamet)	H2 Blocker	Avoid when possible: CYP450 inhibitor, gynecomastia, impotence, confusion in elderly.
Nizatidine (Axid)	H2 Blocker	Similar to famotidine. Minimal drug interactions.

 **Ranitidine (Zantac) Note:** Withdrawn from U.S. market (NDMA contamination concern). If seen on an older NCLEX question bank, recognize it as an H2 blocker, but famotidine has replaced it clinically.

Key Class Differences to Remember:

- ▶ **1st-Gen (crosses BBB):** sedating, anticholinergic, short-acting, useful for acute symptoms + sleep + N/V + EPS
- ▶ **2nd-Gen (minimal BBB):** non-sedating, minimal anticholinergic, long-acting, for chronic allergy control
- ▶ **H2 Blockers (GI):** decrease gastric acid; famotidine preferred over cimetidine for safety