NCLEX-RN 2026 · NGN/NCJMM ALIGNED · PHARMACOLOGY · CNS / PAIN

Moderate *Opioids*

Codeine · Hydrocodone · Tramadol — high-yield clinical judgment for the licensure exam and bedside safety.

HIGH-ALERT MEDICATIONS

ANTIDOTE: NALOXONE

RR < 12 = HOLD

Most-Tested Drugs in This Class

GENERIC · BRAND · SCHEDULE

Codeine

CODEINE SULFATE · W/ APAP = TYLENOL #3, #4

- **Prodrug** → CYP2D6 → morphine
- Antitussive + analgesic
- ⚠ **Black Box:** ultra-rapid metabolizers
- Contraindicated <12 yrs & breastfeeding

Schedule II (alone) · III–V combo

Hydrocodone

VICODIN · NORCO · LORTAB · HYCET

- Almost always combined w/ **acetaminophen**
- Watch **APAP ceiling: 4 g/day** (3 g liver dz)
- Antitussive in some products
- Active metabolite: hydromorphone

Schedule II

Tramadol

ULTRAM · CONZIP · ULTRACET (W/ APAP)

- **Dual MOA:** μ-opioid + SNRI
- ⚠ **Seizure risk** — esp. w/ SSRI/TCA/bupropion
- ⚠ **Serotonin syndrome** risk
- Contraindicated with MAOIs

Schedule IV

1 Drug Overview

WHY WE GIVE THEM · HIGH-YIELD INDICATIONS

Class Definition

- **Moderate-strength opioid agonists** — partial μ-receptor activity vs. morphine
- Treat **moderate to moderately severe pain** (acute, post-op, chronic)
- Codeine + hydrocodone: also **antitussive** (cough suppression)
- Often combined w/ acetaminophen or ibuprofen for synergy
- All carry CNS DEPRESSION risk

Key Indications

- Post-surgical & dental pain
- Musculoskeletal injury, fractures
- Chronic pain (cancer, neuropathy — tramadol)
- Persistent dry cough (codeine, hydrocodone)
- Bridge therapy when NSAIDs/APAP alone insufficient
- Diarrhea (rare, off-label)

2 Mechanism of Action

HOW IT CHANGES PHYSIOLOGY

Codeine: Prodrug → liver CYP2D6 metabolism → *morphine* → binds μ-receptors in CNS → ↓ pain transmission, ↓ cough reflex.

Hydrocodone: Direct μ-agonist → CYP2D6 converts portion → hydromorphone (more potent) → ↓ ascending pain pathway, ↑ pain threshold.

Tramadol: Weak μ-agonist + inhibits serotonin/norepinephrine reuptake (SNRI-like) → dual analgesic effect → also lowers seizure threshold.

`Opioid binds μ-receptor` → `↓ substance P` → `↓ ascending pain signal` → `↑ pain tolerance` → `CNS depression`

Why it matters: *The same μ-receptor that relieves pain also depresses the brainstem respiratory center. Analgesia and respiratory depression are linked — they cannot be separated.*

3 Therapeutic Effects

WHAT TELLS YOU IT'S WORKING

- **Pain rating drops by ≥ 2 points** on 0–10 scale within 30–60 min PO (faster IV/IM)
- Patient verbalizes relief; able to participate in care, ambulate, deep breathe, cough
- Improved sleep, appetite, mood
- **Cough suppression** (codeine, hydrocodone) — fewer episodes, restful sleep
- Vital signs *stable* — RR ≥ 12, SpO_2 ≥ 92%, normotensive
- Patient drowsy but **arousable** (Pasero Sedation Scale = 1–2)

4 Side Effects & Adverse Reactions

COMMON VS. LIFE-THREATENING

✓ Common (expected)

- **Constipation** — does NOT improve with tolerance
- Sedation, dizziness, drowsiness
- Nausea & vomiting (early days)
- Pruritus (histamine release, NOT allergy)
- Dry mouth
- Mild orthostatic hypotension
- Urinary retention
- Miosis (pinpoint pupils)

🚨 Serious / Life-Threatening

- **Respiratory depression** (RR < 12) — #1 killer
- **Apnea, coma, death** — opioid toxicity triad: pinpoint pupils + ↓RR + coma
- **Seizures** — tramadol (esp. w/ SSRIs, TCAs, bupropion, ↓ renal fx)
- **Serotonin syndrome** — tramadol + serotonergics (HTN, hyperthermia, clonus, agitation)
- **Hepatotoxicity** — combo APAP > 4 g/day (hydrocodone/codeine combos)
- **Neonatal death** — codeine in CYP2D6 ultra-rapid metabolizer mothers
- Severe hypotension, bradycardia
- Physical dependence, tolerance, OUD
- QT prolongation (high-dose tramadol)

5 Priority Nursing Considerations

ASSESS · MONITOR · HOLD · NOTIFY

⛔ HOLD & NOTIFY PROVIDER IF...

RR < 12	SpO_2 < 90%	SBP < 90	Pasero ≥ 3
RESP RATE	PULSE OX	HYPOTENSION	SEDATION

Pasero Opioid-Induced Sedation Scale (POSS): 1 = awake/alert · 2 = slightly drowsy, easy to arouse · **3 = frequently drowsy, drifts off mid-conversation (HOLD)** · 4 = somnolent, minimal response (HOLD + naloxone).

→ Assess & Monitor

- ASSESS Pain (0–10) *before & 1 hr after* dose
- ASSESS RR, SpO_2, BP, HR, sedation level
- MONITOR Bowel function — start stool softener day 1
- MONITOR Urine output (retention)
- MONITOR LFTs if combo w/ APAP

⛔ Contraindications

- **Codeine:** children < 12, post-T&A < 18, breastfeeding mothers
- **Tramadol:** children < 12, MAOI use, seizure d/o, head injury, ↑ ICP
- Severe respiratory disease (asthma, COPD exacerbation)
- Paralytic ileus, bowel obstruction
- Hypersensitivity / opioid allergy
- Acute alcohol intoxication, head trauma

⚠ High-Yield Drug Interactions

- FATAL **+ Benzodiazepines / alcohol / sedatives** → synergistic respiratory depression (Black Box)
- FATAL **Tramadol + MAOI** → hypertensive crisis, serotonin syndrome
- SEIZURE **Tramadol + SSRI / SNRI / TCA / bupropion** → ↓ seizure threshold
- SEROTONIN **Tramadol + triptans, linezolid, St. John's Wort**

- CYP2D6 **Codeine/hydrocodone + fluoxetine, paroxetine, bupropion** → ↓ analgesia
- LIVER Multiple APAP-containing products → hepatotoxicity

6 Labs & Diagnostics

CRITICAL VALUES & WHAT THEY MEAN

- **LFTs (AST, ALT, bilirubin):** baseline + periodic if APAP combos · ALT > 3× ULN = hold + notify
- **Renal function (BUN, Cr, GFR):** tramadol is renally cleared — dose-adjust if CrCl < 30 mL/min (↑ seizure risk)
- **CBC:** baseline; long-term opioid use can cause anemia
- **Serum APAP level:** if suspected overdose of combo product (toxic > 150 mcg/mL at 4 hr)
- **ABG / SpO_2 continuous:** if high-risk pt — $PaCO_2$ > 45 = hypoventilation
- **Urine drug screen:** baseline & routine for chronic pain contracts
- **ECG:** high-dose tramadol — watch QTc prolongation
- **Pregnancy test:** before initiation — opioids cross placenta, neonatal abstinence syndrome

7 Administration & Safety

ROUTE, TIMING, HIGH-ALERT PRECAUTIONS

Routes & Timing

- **PO (most common)** — onset 30–60 min, peak 1–2 hr
- Tramadol IR: q4–6 h · ER: once daily — **do NOT crush/split ER**
- Codeine: IR tabs q4–6 h, max 360 mg/day
- Hydrocodone/APAP: q4–6 h — count APAP < 4 g/day total
- Give with food if GI upset
- Reassess pain 60 min post-PO, 30 min post-IV

High-Alert Precautions

- HIGH-ALERT Two-nurse verification per facility policy
- PCA "PCA by proxy" prohibited — only patient pushes
- Have **naloxone (Narcan) readily available**
- Bed in low position, side rails ↑, fall precautions
- Continuous SpO_2 + capnography for opioid-naïve / OSA pts
- Lock all narcotics in Pyxis; waste with witness
- Use lowest effective dose for shortest duration (CDC guideline)

8 Patient Education

WHAT THE PATIENT MUST KNOW

- **NO alcohol** + no benzos / sleep aids / muscle relaxants — fatal respiratory depression
- **NO driving / heavy machinery** until you know how it affects you
- **Take w/ food** if nausea; sit/stand slowly (orthostasis)
- **Increase fiber + fluids + ambulation** — start stool softener (docusate) day 1
- **Read OTC labels** — many cold/flu meds contain APAP; do not double up
- **Do NOT crush, chew, or split ER tablets** (life-threatening overdose)
- **Do NOT stop abruptly** after long-term use → withdrawal (flu-like, anxiety, abd cramps)
- **Take only as prescribed** — addiction risk; lock medication; never share
- **Keep a naloxone (Narcan) kit at home**; teach family to call 911 + give it
- **Call 911** if breathing < 10/min, can't wake person, blue lips/fingertips
- Pregnant or breastfeeding? **Tell your provider immediately** (esp. codeine)
- Tramadol: report tremor, agitation, sweating, fever — possible serotonin syndrome

9 NCLEX Test Traps

WHERE STUDENTS LOSE POINTS

TRAP 1 · "First sign of opioid toxicity = respiratory depression"

*FALSE. The earliest sign is **increasing sedation**. Respiratory depression follows. Always assess sedation FIRST — it's your warning before the RR drops.*

TRAP 2 · "Tramadol is safer because it's Schedule IV"

*FALSE. Tramadol carries unique risks: **seizures + serotonin syndrome**. It interacts with SSRIs, TCAs, MAOIs, and lowers seizure threshold. Schedule does NOT equal safety.*

TRAP 3 · "Codeine is fine for the breastfeeding mom"

*FALSE. Ultra-rapid CYP2D6 metabolizers convert codeine to dangerously high morphine levels in breast milk → **infant respiratory arrest & death**. Black Box.*

TRAP 4 · "Itching = allergic reaction, hold the drug"

*USUALLY FALSE. Pruritus is **histamine release**, not true allergy. Treat with antihistamine; do NOT label allergic unless rash + airway/anaphylaxis features.*

TRAP 5 · "Constipation will go away with tolerance"

*FALSE. Patients build tolerance to sedation, nausea, euphoria — but **NEVER** to constipation. Bowel regimen is mandatory from day 1.*

TRAP 6 · "Give a second dose of naloxone and you're done"

*FALSE. Naloxone half-life (30–90 min) is **shorter** than most opioids → re-sedation likely. Monitor min. 2 hours; repeat doses or drip may be needed.*

TRAP 7 · "RR is 14, pt is sleepy — give the next dose"

*FALSE. **Sedation precedes respiratory depression**. A drowsy/somnolent patient with a "normal" RR is the highest-risk window. Hold and reassess.*

TRAP 8 · Two combo products at home

> *A patient on Vicodin (hydrocodone/APAP) who also takes Tylenol PM and DayQuil can quickly exceed **4 g APAP/day → hepatotoxicity**. Always teach label reading.*

10 Memory Boosters

MNEMONICS & PATTERN RECOGNITION

Opioid Toxicity Triad

"COMA • PINPOINT • ↓RR"

- **C** oma / unresponsive
- **P** inpoint pupils (miosis)
- **R** espiratory depression (< 12)

If you see all 3 → think opioid OD → naloxone.

Common Side Effects • "BREATHES"

B-R-E-A-T-H-E-S

- **B** radypnea / Bradycardia
- **R** R < 12
- **E** uphoria / dependence
- **A** pnea
- **T** olerance & constipation (T for "Tight gut")
- **H** ypotension
- **E** ye pinpoint (miosis)
- **S** edation (FIRST sign!)

Hold Criteria • "STOP"

S-T-O-P

- **S** edation (Pasero ≥ 3)
- **T** oo low RR (< 12)
- **O** $_2$ sat drop (< 90%)
- **P** ressure low (SBP < 90)

Tramadol's Unique Risks • "TRAM"

T-R-A-M

- **T** hreshold for seizures lowered
- **R** enal dose adjustment needed
- **A** void MAOIs / SSRIs
- **M** ay cause serotonin syndrome

Naloxone Reminder • "NARC"

Patient Teaching • "SAFE"

N-A-R-C

- **N** aloxone reverses opioids (μ antagonist)
- **A** cts fast (1–2 min IV)
- **R** e-sedation possible (short ½-life)
- **C** ontinuous monitoring × 2 hr min

S-A-F-E

- **S** tool softener day 1
- **A** void alcohol/benzos
- **F** all precautions / no driving
- **E** nd slowly — taper, never stop abrupt

Drug Class Comparison

CODEINE VS. HYDROCODONE VS. TRAMADOL

FEATURE	CODEINE	HYDROCODONE	TRAMADOL
DEA Schedule	II (alone) · III–V (combo)	II	IV
Mechanism	Prodrug → morphine via CYP2D6	Direct μ-agonist; CYP2D6 → hydromorphone	μ-agonist **+ SNRI** (dual)
Common Brands	Tylenol #3 / #4	Vicodin · Norco · Lortab	Ultram · ConZip · Ultracet
Antitussive?	✓ Yes (gold standard)	✓ Yes	✕ No
#1 Unique Risk	**Ultra-rapid metabolizer death** in kids/breastfed infants	**APAP hepatotoxicity** (combo products)	**Seizures + serotonin syndrome**
Pediatric Use	⛔ Contraindicated < 12 yrs; < 18 post-T&A	⚠ Caution; avoid < 6 yrs cough use	⛔ Contraindicated < 12 yrs
Breastfeeding	⛔ Contraindicated (Black Box)	⚠ Avoid; safer alternatives preferred	⛔ Avoid (FDA warning)
Renal Adjust	Reduce in severe impairment	Reduce in severe impairment	**Required** if CrCl < 30
Top Drug Interaction	SSRIs (↓ analgesia via CYP2D6)	Other APAP products → liver	**SSRI / MAOI / TCA / bupropion**
Onset (PO)	30–60 min	10–30 min	30–60 min
NCLEX Pearl	"Don't give to a nursing mom"	"Count the Tylenol — < 4 g/day"	"Not safer — seizures + serotonin"

★ NGN / NCJMM · CLINICAL JUDGMENT SNAPSHOT

The *3 Questions* the Exam Will Ask You.

When the scenario gives you a moderate opioid, your thinking should snap to these three answers — every time.

Q1 · #1 PRIORITY RISK

"What is the most dangerous adverse effect of this drug?"

Respiratory depression → arrest.

The μ-receptors that relieve pain also depress the brainstem respiratory center. Risk is highest in opioid-naïve, elderly, OSA, COPD, or polypharmacy (benzos, alcohol) patients. Always have **naloxone** at the bedside.

Q2 · WHAT HARMS FIRST

"What will harm the patient before anything else?"

Sedation — not low RR.

Increasing somnolence is the EARLIEST warning sign. By the time RR drops below 12, the patient has been over-sedated for some time. Use the Pasero scale: **POSS ≥ 3 = HOLD the dose, STOP the PCA, notify the provider.**

Q3 · FIRST NURSING ACTION

"RR is 8, patient is unarousable — what do you do FIRST?"

Stimulate & support airway → call rapid response → naloxone.

Order: (1) *Stop the opioid*, (2) call for help / rapid response, (3) open airway, give O_2 & bag-mask if needed, (4) **Naloxone 0.4–2 mg IV/IM/intranasal**, repeat q2–3 min PRN, (5) continuous monitoring × 2 hr (re-sedation).