NGN NCLEX 2026 VISUAL STUDY LIBRARY · PHARMACOLOGY

SNRIs

Serotonin–Norepinephrine Reuptake Inhibitors — mechanism, side effects, contraindications, nursing care & teaching, drug-by-drug.

PSYCHIATRIC PHARM | MOOD / ANXIETY | PAIN MODULATION

SOURCE NOTE: SNRIs were not present in the uploaded personal flashcard set. Content compiled from standard NCLEX references — *Saunders Comprehensive Review for the NCLEX-RN (2026)*, *ATI RN Pharmacology Made Easy*, *Lippincott Illustrated Reviews: Pharmacology*, and FDA prescribing information for venlafaxine, desvenlafaxine, duloxetine, levomilnacipran, and milnacipran.

1 Definition & Overview

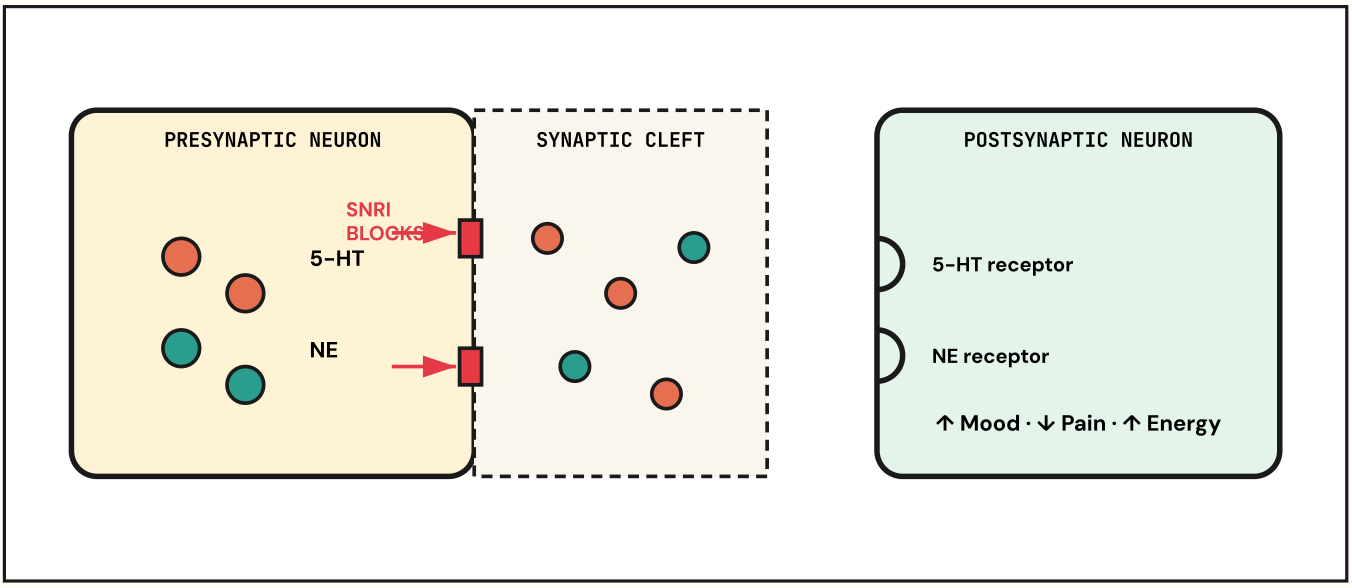
WHAT THEY ARE · WHAT THEY TREAT

- **SNRI = Serotonin–Norepinephrine Reuptake Inhibitor.** Second-generation antidepressant that blocks reuptake of **both** serotonin (5-HT) **and** norepinephrine (NE) at the synapse — increasing the availability of both neurotransmitters.
- **Why two neurotransmitters matter:** Serotonin lifts mood & reduces anxiety. Norepinephrine boosts energy, focus, and modulates descending pain pathways — which is why SNRIs treat **both depression and chronic pain**.
- **Primary indications:** Major Depressive Disorder (MDD), Generalized Anxiety Disorder (GAD), panic disorder, social anxiety disorder, diabetic peripheral neuropathy, fibromyalgia, chronic musculoskeletal pain, and vasomotor symptoms of menopause.

2 Mechanism (Simplified)

HOW SNRIS WORK IN THE SYNAPSE

- In depression/anxiety, **5-HT and NE levels are low** at the synapse → flattened mood, anhedonia, pain amplification.
- SNRIs **block the reuptake transporters (SERT & NET)** on the presynaptic neuron → neurotransmitters stay longer in the cleft → more binding at postsynaptic receptors.
- Lower doses are **more serotonergic**; higher doses recruit **noradrenergic** effects (this is why BP rises at higher doses of venlafaxine).
- Onset of mood benefit: **2–4 weeks**. Full effect: **4–6 weeks**. Pain relief may occur sooner.



3 The SNRIs — Drug-by-Drug

EACH AGENT · INDICATION · KEY TEACHING

Venlafaxine

BRAND: EFFEXOR / EFFEXOR XR · ORAL · IR & ER FORMS

INDICATIONS	MDD, GAD, panic disorder, social anxiety disorder. Off-label: hot flashes/vasomotor menopausal symptoms, neuropathic pain.
MECHANISM	Low dose = mostly serotonergic. **Higher doses (>150 mg/day) = strong NE effect** — explains dose-related BP rise.
WATCH FOR	**Hypertension (dose-dependent)**, nausea, dizziness, insomnia, sexual dysfunction, sweating, severe discontinuation syndrome (short half-life).
TEACH	Take with food. **Do not crush/chew XR** — swallow whole. Check BP regularly. **Never stop abruptly** — taper to avoid withdrawal.

Desvenlafaxine

BRAND: PRISTIQ · ORAL · ACTIVE METABOLITE OF VENLAFAXINE

INDICATIONS	MDD. Off-label: vasomotor symptoms of menopause.
MECHANISM	The active metabolite — fewer CYP450 drug interactions than venlafaxine. Similar dual reuptake blockade.
WATCH FOR	Nausea, dizziness, hyperhidrosis, BP elevation, sexual dysfunction. **Hyponatremia/SIADH risk** in older adults.
TEACH	May take with or without food. Swallow whole. Report dizziness, confusion, or weakness (possible low sodium).

Duloxetine

BRAND: CYMBALTA · ORAL · DELAYED-RELEASE CAPSULE

INDICATIONS	MDD, GAD, **diabetic peripheral neuropathy**, **fibromyalgia**, chronic musculoskeletal pain, stress urinary incontinence (off-label in US).
MECHANISM	Balanced 5-HT and NE reuptake inhibition across the dose range — strong pain-modulating effect.
WATCH FOR	**Hepatotoxicity** — monitor LFTs, avoid in heavy alcohol use or liver disease. Nausea, dry mouth, constipation, fatigue, decreased appetite.
TEACH	**Do NOT crush or chew** the capsule — disrupts delayed release. **Avoid alcohol.** Report yellowing skin/eyes, dark urine, RUQ pain.

Levomilnacipran

BRAND: FETZIMA · ORAL · EXTENDED-RELEASE CAPSULE

INDICATIONS	MDD only.
MECHANISM	More **NE-selective** than the others — preferentially boosts norepinephrine, which may improve energy and focus.
WATCH FOR	Nausea, constipation, sweating, tachycardia, BP and HR elevation, urinary hesitancy/retention.
TEACH	Swallow whole. Take at the same time daily. Report difficulty urinating or rapid heartbeat.

Milnacipran

BRAND: SAVELLA · ORAL · TWICE-DAILY DOSING

INDICATIONS	**Fibromyalgia only** (in the US — not FDA-approved as an antidepressant). NCLEX trap: it is structurally an SNRI but not marketed for depression in the US.
MECHANISM	More NE-selective; targets pain modulation pathways.
WATCH FOR	Nausea, headache, hypertension, tachycardia, hot flashes, palpitations.
TEACH	Take twice daily. Black box: increased suicidality in patients <25. Monitor BP at home.

4 Side Effects & Red Flags

COMMON · SERIOUS · LIFE-THREATENING

COMMON / EXPECTED

- **Nausea** (most common — usually subsides in 1–2 weeks)
- Headache, dizziness
- Dry mouth
- Insomnia *or* somnolence
- Sweating (hyperhidrosis)
- Sexual dysfunction (decreased libido, delayed orgasm)
- Decreased appetite, constipation
- Mild ↑ HR and BP

SERIOUS / ADVERSE

- **Serotonin syndrome** — life-threatening
- **Suicidal ideation** — esp. patients <25 yrs (Black Box Warning)
- **Hypertensive crisis** — dose-related (esp. venlafaxine)
- **Hyponatremia / SIADH** — esp. older adults
- **Hepatotoxicity** — duloxetine especially
- **Bleeding risk** — with NSAIDs/warfarin/antiplatelets
- **Mydriasis / angle-closure glaucoma**
- **Seizures** — lower threshold
- **Discontinuation syndrome** if stopped abruptly
- **Mania switch** in undiagnosed bipolar disorder

SEROTONIN SYNDROME — Recognize the 4 H's + ABCs

Hyperthermia · **Hypertension** · **Hyperreflexia / clonus** · **Hallucinations / agitation** + tachycardia, diaphoresis, tremor, N/V/diarrhea, mydriasis. **Most often triggered when SNRI combined with MAOI, SSRI, triptans, tramadol, linezolid, St. John's wort, or methylene blue.** First action: **STOP the drug** & notify HCP.

DISCONTINUATION SYNDROME — Especially Venlafaxine (short half-life)

Flu-like symptoms, dizziness, "electric-shock" or "brain zap" sensations, insomnia, nausea, irritability, vivid dreams. Begins within 1–3 days of abrupt stop. **Always taper over weeks.**

5 Priority Nursing Interventions

ABC FRAMEWORK · SAFETY · PRIORITIZATION

AIRWAY / BREATHING

- Monitor for serotonin syndrome → respiratory compromise possible
- Assess for allergic reaction / angioedema
- Watch for seizure activity (lowered threshold)

CIRCULATION

- **Baseline + ongoing BP & HR** — especially venlafaxine
- Hold & notify HCP if BP rises significantly above baseline
- Assess for bleeding (with NSAIDs/anticoagulants)
- Monitor ECG if cardiac history (QT effects in some)

SAFETY

- **Suicide assessment** — at start, dose changes, & weekly first month
- Fall precautions (dizziness, orthostasis)
- Confirm **no MAOI within 14 days** before starting
- Verify no contraindicated drugs (triptans, tramadol, linezolid)

- **Assess** baseline mood, suicide risk, sleep, appetite, weight, sexual function, pain level.
- **Monitor** LFTs (especially duloxetine), serum sodium (especially older adults), CBC if bleeding.
- **Administer** with food to reduce GI upset; give morning dose if insomnia, evening if sedating.
- **Evaluate** response over 2–4 weeks — therapeutic effect is **not immediate**; do not increase based on a single bad day.
- **Reinforce** never to stop abruptly — taper schedule must come from HCP.

6 Pharmacology Comparison

QUICK REFERENCE TABLE — ALL 5 SNRIS

DRUG	BRAND	PRIMARY USE	DISTINGUISHING FEATURE	KEY CAUTION
Venlafaxine	Effexor / Effexor XR	MDD, GAD, panic, social anxiety	Dose-dependent NE effect	↑ BP at higher doses; severe withdrawal — taper carefully
Desvenlafaxine	Pristiq	MDD	Active metabolite — fewer CYP interactions	Hyponatremia / SIADH in elderly
Duloxetine	Cymbalta	MDD, GAD, diabetic neuropathy, fibromyalgia, chronic pain	Strongest pain-modulating SNRI	Hepatotoxicity — avoid alcohol & liver disease; monitor LFTs
Levomilnacipran	Fetzima	MDD	More NE-selective — boosts energy/focus	Urinary hesitancy, tachycardia, ↑ BP
Milnacipran	Savella	Fibromyalgia (US — not approved for MDD here)	Twice-daily dosing	↑ BP/HR; black box suicidality <25

7 Contraindications & Cautions

WHO SHOULD NOT TAKE SNRIS

ABSOLUTE CONTRAINDICATIONS

- **MAOI within last 14 days** (either direction) — fatal serotonin syndrome risk
- Concurrent use with **linezolid** or **IV methylene blue**
- Hypersensitivity to the drug
- **Uncontrolled narrow-angle glaucoma**
- Duloxetine: severe hepatic impairment, end-stage renal disease (CrCl <30), chronic heavy alcohol use

USE WITH CAUTION

- **Bipolar disorder** — may precipitate mania
- Seizure disorder (lowered threshold)
- Bleeding disorders or on NSAIDs/anticoagulants/antiplatelets
- Pre-existing **hypertension** (esp. venlafaxine)
- Cardiac disease — recent MI, unstable angina
- Pregnancy & lactation — risk vs. benefit; neonatal withdrawal possible if taken in 3rd trimester
- Older adults — hyponatremia, falls, fractures
- Diabetes — duloxetine may alter glycemic control

8 NCLEX Test Traps

WRONG-VS-RIGHT · WHAT THE TEST IS ASKING

✕ TRAP	→	✓ CORRECT
"Patient says SNRI isn't working after 5 days — increase dose."	→	Educate that **full effect takes 2–4 weeks**; continue current dose; monitor for suicidality & side effects.
"Patient wants to stop because side effects are gone and they feel better — okay to discontinue."	→	**Never stop abruptly.** Must taper under HCP guidance to avoid discontinuation syndrome.
"Patient on venlafaxine reports headache and BP 158/96 — give acetaminophen."	→	**Notify HCP.** Venlafaxine causes dose-related HTN — sustained elevation may require dose change or alternative.
"Patient on duloxetine reports nausea and fatigue — reassure it will pass."	→	Check for **RUQ pain, jaundice, dark urine** — duloxetine can cause hepatotoxicity. Notify HCP & check LFTs.
"Patient just finished a 7-day phenelzine course — start duloxetine today."	→	**Wait 14 days** between an MAOI and starting an SNRI — and 5–7 days after stopping the SNRI before starting an MAOI.
"Patient on venlafaxine adds St. John's wort to feel better faster — that's a safe natural supplement."	→	St. John's wort + SNRI = **serotonin syndrome risk**. Same risk with triptans (sumatriptan), tramadol, dextromethorphan.
"Patient newly on SNRI for depression begins giving away possessions and seems peaceful — sign the drug is working."	→	**Suicide red flag.** Sudden calm and giving away belongings can signal a finalized plan. Assess and protect immediately.

9 Patient & Family Education

WHAT TO TEACH BEFORE DISCHARGE

- **Be patient.** It takes **2–4 weeks** to feel meaningful improvement and up to **6 weeks** for full effect.
- **Never stop suddenly.** Even one missed dose of venlafaxine can cause withdrawal. Always taper with your provider.
- **Take with food** to reduce nausea. Duloxetine and venlafaxine ER capsules must be swallowed whole — do not crush, chew, or open.
- **Avoid alcohol** — especially with duloxetine (liver risk) and overall (increases CNS depression).
- **Check your blood pressure** at home weekly during dose changes — particularly with venlafaxine.
- **Watch for mood changes.** Report worsening depression, new anxiety, agitation, panic, hostility, or any thoughts of self-harm — especially in the first 1–2 months and after dose changes.
- **Tell every provider** you take an SNRI — including dentists, urgent care, ER. Many common drugs (triptans for migraines, tramadol, certain cough medicines, linezolid antibiotics, herbal St. John's wort) can cause a dangerous reaction.
- **Use caution with NSAIDs and aspirin** — increases bleeding risk. Report unusual bruising, nosebleeds, or blood in stool/urine.
- **Rise slowly** from sitting or lying to prevent dizziness and falls.
- **Stay hydrated** — but if you feel confused, weak, or have a headache, get checked for low sodium (especially older adults).
- **Pregnancy/breastfeeding:** Discuss risks vs. benefits. Do not stop without HCP guidance — untreated depression carries its own risks to mother and baby.
- **If you have diabetes** (duloxetine): monitor blood glucose more closely — control may shift.

10 Memory Boosters

MNEMONICS · ASSOCIATIONS · PATTERNS

FINISH

SNRI Discontinuation Syndrome

- **F** Flu-like symptoms
- **I** Insomnia (vivid dreams)
- **N** Nausea
- **I** Imbalance (dizziness, vertigo)
- **S** Sensory disturbances ("brain zaps")
- **H** Hyperarousal (anxiety, agitation)

HARMED

Serotonin Syndrome Cues

- **H** Hyperthermia
- **A** Autonomic instability (BP/HR swings)
- **R** Rigidity / clonus / hyperreflexia
- **M** Mental status changes (agitation, confusion)
- **E** Excessive sweating & tremor
- **D** Diarrhea & GI distress

"V·D·D·L·M" — The 5 SNRIs

- **V** Venlafaxine (Effexor) — the prototype; watch BP
- **D** Desvenlafaxine (Pristiq) — its active metabolite
- **D** Duloxetine (Cymbalta) — depression + pain; liver risk
- **L** Levomilnacipran (Fetzima) — MDD; more NE
- **M** Milnacipran (Savella) — fibromyalgia only (in US)

Pattern Cue: "S & N"

- **S** Serotonin → mood, anxiety, pain perception
- **N** Norepinephrine → energy, focus, BP elevation

→ More NE on board = **higher BP** = check venlafaxine dose-dependent HTN

11 NCJMM Clinical Judgment Scenario

SIX-STEP NEXT GEN NCLEX WALK-THROUGH

Scenario: *A 42-year-old client with MDD has been taking* ***venlafaxine ER 150 mg*** *for 6 weeks. She presents to the clinic reporting that her depression "lifted last week" but now she feels "jittery, hot, my heart's racing." She mentions she added a sumatriptan tablet two hours ago for a migraine.* ***VS: T 38.6 °C (101.5 °F), HR 124, BP 168/98, RR 22, SpO$_2$ 96%.*** *On exam: diaphoretic, tremulous, dilated pupils, hyperactive deep tendon reflexes, sustained clonus at the ankles. She is anxious and oriented but speaking rapidly.*

STEP 1 · RECOGNIZE CUES

What stands out?

Hyperthermia (38.6 °C), tachycardia (124), hypertension (168/98), tachypnea, diaphoresis, tremor, mydriasis, **hyperreflexia with sustained clonus**, agitation. Recent addition of a **triptan** to an established SNRI.

STEP 2 · ANALYZE CUES

What's the pattern?

The triad of **autonomic instability + neuromuscular excitability + altered mental status** following the addition of a serotonergic drug (sumatriptan) to an SNRI is classic for **serotonin syndrome**. Clonus + hyperreflexia is the most specific finding.

STEP 3 · PRIORITIZE HYPOTHESES

Most likely problem?

#1 Serotonin syndrome from SNRI + triptan interaction. Rule out: hypertensive crisis alone, anxiety/panic attack, hyperthyroid crisis, sepsis — none explain the clonus & hyperreflexia in this drug context.

STEP 4 · GENERATE SOLUTIONS

What should be done?

STOP the venlafaxine immediately. No more triptan. Transfer to ED for monitoring. Anticipate: IV fluids, cooling measures, benzodiazepines for agitation/rigidity, cyproheptadine (serotonin antagonist) in moderate-to-severe cases, continuous cardiac monitoring. Avoid all serotonergic drugs.

STEP 5 · TAKE ACTION

First nursing actions?

1) **Hold the SNRI dose & notify HCP STAT.** 2) Activate ED transfer / rapid response. 3) Initiate cooling (remove blankets, cool environment). 4) Continuous VS/cardiac monitoring. 5) Establish IV access — anticipate fluid bolus & benzodiazepine. 6) Maintain airway readiness — rigidity can compromise breathing.

STEP 6 · EVALUATE OUTCOMES

Did it work?

Improvement = temperature trending down (<38 °C), HR <100, BP returning toward baseline, resolution of clonus and hyperreflexia, mental status clearing. Worsening = persistent hyperthermia >40 °C, seizures, rhabdomyolysis (↑ CK, dark

> urine), DIC, respiratory failure → escalate to ICU. Document drug-drug interaction in chart; coordinate with team on safe re-initiation plan and patient teaching about the triptan interaction.

END OF CARD · NGN NCLEX 2026

SNRIs — Block two transporters. Lift mood. Watch the pressure.

Next-up suggestions in this cluster: **SSRIs · Tricyclic Antidepressants (TCAs) · MAOIs · Atypical Antidepressants (bupropion, mirtazapine, trazodone) · Serotonin Syndrome (standalone) · Lithium & Mood Stabilizers · Anxiolytics (benzodiazepines/buspirone) · Antipsychotics — Typical vs Atypical.**