



SSRIs & SNRIs

Selective Serotonin Reuptake Inhibitors | Serotonin-Norepinephrine Reuptake Inhibitors

Drug Class: Antidepressants • System: Neurological / Psychiatric



1. DRUG OVERVIEW — Why We Give It

SSRI EXAMPLES (Generic / Brand):

- **Fluoxetine** (Prozac) — longest half-life, activating
- **Sertraline** (Zoloft) — most prescribed; take with food
- **Paroxetine** (Paxil) — most sedating; **pregnancy Cat D**
- **Citalopram** (Celexa) — QT prolongation risk
- **Escitalopram** (Lexapro) — fewest side effects
- **Fluvoxamine** (Luvox) — OCD focus

SNRI EXAMPLES (Generic / Brand):

- **Venlafaxine** (Effexor) — dose-dependent HTN
- **Duloxetine** (Cymbalta) — also for pain / DM neuropathy
- **Desvenlafaxine** (Pristiq)
- **Levomilnacipran** (Fetzima)

KEY INDICATIONS:

- Major Depressive Disorder (MDD) — **first-line**
- Generalized Anxiety Disorder (GAD)
- Panic Disorder, Social Anxiety, PTSD
- Obsessive-Compulsive Disorder (OCD)
- **SNRI only:** fibromyalgia, diabetic neuropathy, chronic pain (duloxetine)



2. MECHANISM OF ACTION — Simplified

SSRI PATHWAY:

- Block serotonin (5-HT) reuptake at presynaptic neuron
- → ↑ serotonin in synaptic cleft
- → enhanced post-synaptic 5-HT stimulation
- → improved mood, ↓ anxiety, ↓ intrusive thoughts

SNRI PATHWAY:

- Block BOTH serotonin AND norepinephrine reuptake
- → ↑ 5-HT + ↑ NE in synaptic cleft
- → improved mood + pain modulation + ↑ energy



ONSET RULE:

- Neurotransmitter levels ↑ within hours, but **therapeutic effect takes 4–6 weeks**
- → Receptor downregulation is the slow step — not the drug level

3. THERAPEUTIC EFFECTS — What 'Working' Looks Like

- **Mood lifts** — less hopelessness, improved outlook
- **Anxiety decreases** — fewer panic attacks, calmer affect
- **Sleep normalizes** — easier to fall / stay asleep
- **Appetite returns** — normal eating patterns
- **↑ Energy and motivation** — resumes ADLs and hobbies
- **↓ Intrusive / ruminative thoughts** (OCD, PTSD)
- **SNRI**: measurable pain relief (neuropathy, fibromyalgia)

⚠ **CRITICAL NCLEX POINT:**

- **Energy improves BEFORE mood** → suicide risk ↑ in first 1–4 weeks
- The patient now has the drive to act on prior suicidal thoughts

4. SIDE EFFECTS & ADVERSE REACTIONS

COMMON (Usually transient — 2–4 weeks):

- GI: **nausea**, diarrhea, dry mouth
- **Sexual dysfunction** — ↓ libido, anorgasmia, ED
- Headache, dizziness
- Insomnia (fluoxetine) OR sedation (paroxetine)
- Weight changes (↑ or ↓)
- Tremor, jitteriness, sweating

🚨 **SERIOUS / LIFE-THREATENING:**

- **Serotonin Syndrome** — medical emergency
- **Suicidal ideation** — BLACK BOX WARNING (esp. <25 yo, first 4 wks)
- **SIADH / hyponatremia** — esp. elderly ($\text{Na}^+ < 135$)
- **↑ Bleeding risk** — platelet dysfunction (GI bleed with NSAIDs)
- **QT prolongation** — citalopram (max 40 mg; 20 mg if >60 yo)
- **Discontinuation syndrome** — flu-like, dizziness, 'brain zaps'
- **SNRI: Hypertension** — dose-dependent (venlafaxine)
- **SNRI: Hepatotoxicity** — duloxetine (↑ with ETOH use)
- **Activation of mania** in undiagnosed bipolar disorder

🔥 **SEROTONIN SYNDROME — Know These Signs:**

- **Mental status**: agitation, confusion, restlessness
- **Autonomic**: hyperthermia, tachycardia, HTN, diaphoresis, dilated pupils
- **Neuromuscular**: tremor, **hyperreflexia**, myoclonus, clonus (ankle), rigidity
- GI: nausea, vomiting, diarrhea
- **TREATMENT**: STOP drug → supportive care → cyproheptadine (antidote)

5. PRIORITY NURSING CONSIDERATIONS

→ **ASSESS / MONITOR:**

- **Suicidal ideation — every visit** (esp. first 4 weeks, dose changes, <25 yo)
- Mood, affect, behavior changes
- Vital signs — **BP for SNRIs** (baseline + ongoing)
- Signs of serotonin syndrome
- Signs of hyponatremia (confusion, HA, seizures) — esp. elderly
- Signs of bleeding (bruising, melena, hematuria)
- Weight, sleep, appetite

→ **HOLD / NOTIFY PROVIDER IF:**

- Signs of serotonin syndrome (hyperreflexia, clonus, fever, agitation)
- Na⁺ <135 mEq/L or symptoms of hyponatremia
- BP sustained >140/90 (SNRI) — dose reduction
- QTc >500 ms (citalopram)
- New/worsening suicidal ideation
- Active GI bleed or significant bruising
- Manic switch (bipolar activation)

⊘ **CONTRAINDICATIONS:**

- **MAOI use within 14 days** (5 WEEKS for fluoxetine — long half-life)
- Concurrent linezolid, IV methylene blue
- Known serotonin syndrome history
- Paroxetine + pregnancy (**Cat D — cardiac defects**)
- Uncontrolled narrow-angle glaucoma
- Duloxetine + severe hepatic impairment / heavy ETOH

⚡ **DRUG INTERACTIONS (serotonergic — high risk!):**

- **MAOIs** (phenelzine, selegiline, tranylcypromine)
- **Triptans** (sumatriptan) — migraine meds
- **Tramadol, meperidine, fentanyl** — opioids
- **Linezolid, methylene blue**
- **St. John's Wort** (herbal)
- **Lithium, buspirone, other SSRIs/SNRIs, TCAs**
- **Dextromethorphan** (OTC cough)
- **NSAIDs / warfarin / antiplatelets** → bleeding risk

6. LABS & DIAGNOSTICS

LAB / TEST	NORMAL	WHY / ABNORMAL MEANS
Sodium (Na⁺)	135–145 mEq/L	↓ Na ⁺ → SIADH (esp. elderly) → confusion, seizures → HOLD
LFTs (AST/ALT)	<40 U/L	↑ with duloxetine → hepatotoxicity → STOP drug
ECG / QTc	QTc <450 (M) / <470 (F) ms	Citalopram → QT prolongation → Torsades risk
CBC / Platelets	150–400 K/μL	Bleeding risk assessment (esp. with NSAIDs)
BP	<120/80	SNRI → dose-dependent HTN (venlafaxine)
PT/INR	INR 0.8–1.1	↑ bleeding risk if on warfarin
Pregnancy test	Negative	Paroxetine = Cat D; SSRIs → neonatal adaptation

LAB / TEST	NORMAL	WHY / ABNORMAL MEANS
		syndrome
TSH	0.4–4.0 mIU/L	R/O hypothyroidism mimicking depression (baseline)
Glucose	70–99 (fasting)	SSRIs may alter glycemic control (diabetics)

7. ADMINISTRATION & SAFETY

ROUTE & TIMING:

- **PO — once daily**, consistent time each day
- **With food** if GI upset (sertraline — better absorption with food)
- **Morning dose** if activating (fluoxetine, sertraline)
- **Evening dose** if sedating (paroxetine)
- Extended-release forms — **do NOT crush / chew / split**

SAFETY RULES:

- **NEVER stop abruptly** — taper over 2–4 weeks to prevent discontinuation syndrome
- **14-day MAOI washout** before starting SSRI/SNRI (**5 weeks for fluoxetine**)
- **14-day SSRI/SNRI washout** before starting MAOI
- Allow **4–6 weeks** to assess therapeutic response
- Use **lowest effective dose** in elderly (↑ SIADH, falls, bleeding)
- Caution with driving until response known
- No alcohol — ↑ CNS depression + hepatotoxicity (duloxetine)

HIGH-ALERT PRECAUTIONS:

- Suicide risk screening **at every encounter** (esp. first month)
- Citalopram: **max 40 mg/day** (20 mg if >60 yo, hepatic impairment) — QT risk
- Remove means of self-harm if ideation present

8. PATIENT EDUCATION — Teaching Points

MUST KNOW:

- **Full effect takes 4–6 weeks** — do NOT stop early if you feel no change
- **Never stop suddenly** — always taper with provider guidance
- Take at the **same time every day**
- May take with food to reduce nausea
- Sexual side effects are common but often improve / are manageable

SEEK HELP IMMEDIATELY IF:

- **Thoughts of suicide or self-harm**
- **Fever + agitation + muscle twitching** (serotonin syndrome)
- **Unusual bleeding or bruising** (gums, nose, stool, urine)
- **Severe headache, confusion, seizure** (hyponatremia)
- **New mania** — racing thoughts, no sleep, euphoria
- **Rash, swelling** (allergic reaction)

SAFETY TEACHING:

- **Avoid alcohol** — worsens depression + ↑ side effects
- **Avoid St. John's Wort** — causes serotonin syndrome
- Tell **all providers & dentists** you're on this medication
- Avoid NSAIDs — use acetaminophen for pain if possible
- **Carry a med list** (especially for ER visits)
- Use contraception if of childbearing age (esp. paroxetine)
- Rise slowly from sitting (orthostatic hypotension possible)

9. NCLEX TEST TRAPS ⚠️

TRAP #1 — 'The patient says the drug isn't working after 1 week'

- ❌ **WRONG:** "Notify provider to change the medication"
- ✅ **RIGHT:** "It takes **4–6 weeks** for full effect — continue as prescribed"

TRAP #2 — Suicide risk timing

- Risk **INCREASES** in first 1–4 weeks because energy returns **before** mood
- Patient can now ACT on suicidal thoughts they had pre-treatment

TRAP #3 — MAOI washout period

- Standard SSRI/SNRI → MAOI: **14 days**
- **Fluoxetine** → MAOI: **5 WEEKS** (long half-life, active metabolite)
- Missing this = fatal serotonin syndrome

TRAP #4 — Serotonin Syndrome vs NMS

- **Serotonin syndrome:** SEROTONERGIC drug + **hyperreflexia, clonus** (fast onset)
- **NMS:** ANTIPSYCHOTIC drug + **lead-pipe rigidity**, ↑ CK (slow onset, days)

TRAP #5 — 'Safe' OTCs aren't always safe

- **St. John's Wort** → serotonin syndrome
- **Dextromethorphan** (cough) → serotonin syndrome
- **NSAIDs / ibuprofen** → GI bleed risk

TRAP #6 — Pregnancy

- **Paroxetine** = **Category D** (cardiac defects) — AVOID
- Sertraline usually preferred if treatment needed in pregnancy

TRAP #7 — Discontinuation ≠ Addiction

- Flu-like symptoms, brain zaps, dizziness = **discontinuation syndrome**
- NOT addiction or withdrawal — teach patients they're not "hooked"

TRAP #8 — Citalopram ceiling dose

- Max **40 mg/day** adults, **20 mg/day** if >60 yo — QT prolongation

10. MEMORY BOOSTERS — Mnemonics & Patterns

🔑 Serotonin Syndrome — 'SHIVERS'

- **S** — Shivering
- **H** — Hyperreflexia / myoclonus
- **I** — Increased temperature
- **V** — Vital sign instability (↑ HR, ↑ BP)

- **E** — Encephalopathy (confusion, agitation)
- **R** — Restlessness / tremor
- **S** — Sweating / diarrhea

🔑 **SSRI Side Effects — 'SAD SEX'**

- **S** — Sleep disturbance
- **A** — Agitation / anxiety (initial)
- **D** — Diarrhea / GI upset
- **SEX** — Sexual dysfunction

🔑 **Drug-Specific Hooks:**

- **Fluoxetine = Forever** → longest half-life → 5-week MAOI washout
- **Paroxetine = Pregnancy Poison** → Cat D, avoid
- **Citalopram = Cardiac** → QT prolongation → max 40 mg
- **Duloxetine = Double-duty** → depression + neuropathic pain (DM, fibro)
- **Venlafaxine = Vessel-squeezer** → dose-dependent HTN
- **Sertraline = Stomach** → take with food

🔑 **Class Pattern Recall:**

- **'SSRI' = 'Start Slow, Rise slowly, Inform all providers'**
- **4–6 weeks** to work → **2–4 weeks** to taper → **14 days** MAOI washout (5 wks flu)
- **Suicide screen + Serotonin syndrome + Sodium + Sex dysfunction = the 4 S's to watch**



CLINICAL JUDGMENT SNAPSHOT

NCJMM • Priority Thinking • Act First

? **What is the #1 priority risk with SSRIs/SNRIs?**

→ Serotonin syndrome (life-threatening) AND suicidal ideation — both can kill the patient fast if missed.

? **What will harm the patient FIRST?**

→ Serotonin syndrome from a drug combination (MAOI, triptan, tramadol, St. John's Wort). Onset is within hours — hyperthermia, clonus, and autonomic instability can cause death in 24 hrs.

? **What is the FIRST nursing action in a serotonin syndrome scenario?**

→ **STOP the offending drug IMMEDIATELY.**

→ Then: notify provider, initiate cooling, IV fluids, benzodiazepines for agitation, cyproheptadine for antidote, continuous monitoring.

🎯 **ASK BEFORE EVERY DOSE:**

"Any new meds? Any thoughts of self-harm? Any fever or muscle jerking?"



MOST-TESTED DRUGS IN THIS CLASS — Quick Compare

DRUG	CLASS	KEY USE	RED FLAG	NCLEX POINT
Fluoxetine	SSRI	MDD, OCD, Bulimia	Long half-life	5-wk MAOI



DRUG	CLASS	KEY USE	RED FLAG	NCLEX POINT
(Prozac)				washout
Sertraline (Zoloft)	SSRI	MDD, PTSD, Panic, OCD	GI upset	Take with food
Paroxetine (Paxil)	SSRI	MDD, GAD, Panic	Pregnancy Cat D	Most sedating / anticholinergic
Citalopram (Celexa)	SSRI	MDD	QT prolongation	Max 40 mg (20 mg if >60)
Escitalopram (Lexapro)	SSRI	MDD, GAD	Fewer SE profile	Often best-tolerated SSRI
Venlafaxine (Effexor)	SNRI	MDD, GAD, Panic	Dose-dependent HTN	Monitor BP ongoing
Duloxetine (Cymbalta)	SNRI	MDD, DM neuropathy, fibromyalgia	Hepatotoxicity	Avoid with ETOH / liver dz
Desvenlafaxine (Pristiq)	SNRI	MDD	HTN	Active metabolite of venlafaxine



VS SSRI vs SNRI — Key Differences

FEATURE	SSRI	SNRI
Neurotransmitter	Serotonin only	Serotonin + Norepinephrine
Primary use	Depression, anxiety, OCD	Depression + PAIN (neuropathy, fibro)
BP effect	Usually neutral	↑ BP (dose-dependent)
Sexual SE	Common	Common
Serotonin syndrome risk	High with combos	High with combos
Discontinuation	Yes — taper	Yes — MORE severe (esp. venlafaxine)
Hepatotoxicity	Rare	Duloxetine — significant
First-line?	Yes — MDD, anxiety	Yes, esp. if pain + depression

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