Updated September 2026

Duloxetine

Brand names - Cymbalta, Irenka *Oral adult dosing for multiple conditions*

Duloxetine is a serotonin-norepinephrine reuptake inhibitor (SSRI). Its therapeutic mechanism is thought to be related to inhibiting reuptake of both serotonin and norepinephrine, thus increasing availability of both in the CNS.

	Generalized Anxiety Disorder	Major Depressive Disorder	Fibromyalgia	Neuropathic Pain (Diabetes)
Initial Dose	60 mg/day	40-60 mg/day	30 mg/day x 1 week	60 mg/day
Target	60 mg/day	40-60 mg/day	60 mg/day	60 mg/day
Max Dose	120 mg/day	120 mg/day	60 mg/day	60 mg/day

Prescribing Pearls

- Administer delayed-release capsules with or without food and swallow whole.
- Consider a lower starting dose of 30 mg/day in patients with increased sensitivity to medications, hepatic impairment, older age, or tolerability concerns.
- Measure blood pressure before and during treatment. Duloxetine can increase BP and pulse.
- Assess for a history of mania/hypomania and other bipolar-spectrum risk factors. Antidepressants may precipitate a manic, mixed, or hypomanic episode in vulnerable individuals.
- Avoid in patients w/ chronic liver disease, cirrhosis, or severe renal impairment (GFR <30mL/min).
- Common side effects include nausea, constipation, anxiety, insomnia, increased sweating, and decreased appetite. Sexual dysfunction is less common than with SSRIs but may occur.
- Transient anxiety may occur early in treatment; distinguish from worsening of underlying disorder or emerging mania.
- Wait ≤14 days after stopping an MAOI before starting duloxetine. Wait ≤5 days after stopping duloxetine before starting an MAOI. Review other serotonergic rx; monitor for serotonin syndrome.
- Avoid abrupt discontinuation when possible. Gradually taper and monitor for discontinuation symptoms such as dizziness, irritability, anxiety, sensory disturbances, headache, insomnia, or mood change.

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Safety

- **Pregnancy.** Use an individualized risk-benefit assessment. Available published and post-marketing data have not identified a clear duloxetine-associated increase in major birth defects or other adverse developmental outcomes. **Untreated depression and anxiety also carry maternal and pregnancy-related risks.**
  - Late-third-trimester exposure may be associated with neonatal adaptation symptoms, including respiratory distress, feeding difficulty, temperature instability, abnormal muscle tone, tremor, jitteriness, irritability, hypoglycemia, or other symptoms; some infants may require respiratory support, tube feeding, or prolonged hospitalization.
  - SSRI exposure, particularly near delivery, has also been associated with a modest increase in postpartum hemorrhage risk.
- **Lactation.** duloxetine is present in human milk, but available data suggest relatively low infant exposure. Published data remain limited. Monitor breastfed infants for sedation, poor feeding, and poor weight gain, particularly in younger or medically vulnerable infants.
- Suicidality: Monitor for clinical worsening, unusual behavioral changes, and suicidal thoughts, particularly in young adults and around treatment changes.
- Bleeding risk: SNRIs may increase bleeding risk, particularly with NSAIDs, aspirin, antiplatelet therapy, or anticoagulants.
- May cause hyponatremia, particularly in older adults, patients taking diuretics, or volume-depleted patients.
- Hepatic safety: assess for chronic liver disease and substantial alcohol use before treatment. Avoid duloxetine in patients with chronic liver disease or cirrhosis and in patients with substantial alcohol use. Evaluate promptly for jaundice, dark urine, pruritus, right-upper-quadrant pain, or other evidence of significant hepatic dysfunction.
- Drug interactions: avoid potent CYP1A2 inhibitors when possible; potent CYP2D6 inhibitors may increase duloxetine exposure. Duloxetine is also a moderate CYP2D6 inhibitor and may increase concentrations of some TCAs, antipsychotics, beta-blockers, and class 1C antiarrhythmics.

Disclaimer

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