Cymbalta

(duloxetine)

Cymbalta (duloxetine); not controlled

Full Prescribing Information	DailyMed Drug Information

Summary

Cymbalta is a serotonin and norepinephrine reuptake inhibitor supplied as a delayed-release capsule, approved in children for generalized anxiety disorder from 7 years and for juvenile fibromyalgia from 13 years, with further indications in adults only. It has no ADHD indication at any age, and appears in this library because anxiety so often accompanies ADHD. Its distinguishing feature in youth is dual action on mood and pain. Not controlled; brand and generic.

Forms & Strengths

- **Delayed-release capsules:** 20 mg, 30 mg, 40 mg, 60 mg
- **Delayed-release capsules, separate NDA:** 80 mg, 90 mg, 120 mg
- **Delayed-release sprinkle capsules** (Drizalma Sprinkle, separate NDA): 20 mg, 30 mg, 40 mg, 60 mg

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Dosing

- **Age:**
  - Generalized anxiety disorder: 7 y/o and older, and adults
  - Juvenile fibromyalgia: 13 y/o and older
  - Major depressive disorder, diabetic peripheral neuropathic pain, chronic musculoskeletal pain: adults only
- **Onset:** 2 weeks for early effect; 10 to 13 weeks for full response
- **Duration:** continuous with once-daily dosing; steady state at about 3 days
- **Initial Dose:**

    - GAD, 7 to 17 y/o: 30 mg once daily, held for 2 weeks before any increase
    - Juvenile fibromyalgia, 13 to 17 y/o: 30 mg once daily
    - Adults: 60 mg once daily; geriatric adults 30 mg once daily
- **Titration:**
    - GAD, 7 to 17 y/o: 30 mg increments, first no sooner than 14 days, usual range 30 to 60 mg daily
    - Juvenile fibromyalgia, 13 to 17 y/o: single increase to 60 mg once daily on response and tolerability
- **Max Dose:**
    - GAD and MDD, any age: 120 mg/day
    - Fibromyalgia and chronic musculoskeletal pain: 60 mg/day, with no added benefit above 60 mg
- **Considerations:** Avoid in chronic liver disease, cirrhosis, substantial alcohol use, and GFR under 30 mL/min. Never stop abruptly; discontinuation syndrome follows tapered as well as abrupt cessation.

Pharmacology

- **Mechanism:** serotonin and norepinephrine reuptake inhibitor; the full serotonergic action drives both serotonin syndrome and bleeding risk
- **Delivery / Release:** enteric-coated pellets protect an acid-labile drug, so the capsule cannot be crushed, chewed or sprinkled
- **Metabolism:** hepatic via CYP1A2 and CYP2D6; half-life about 12 hours, range 8 to 17. Duloxetine is itself a moderate CYP2D6 inhibitor
- **Class Positioning:** steady state at ages 7 to 17 runs about 30% below adults. Against atomoxetine (Strattera) it adds serotonergic action, analgesia and a discontinuation syndrome

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Indications

- **Generalized Anxiety Disorder** (ICD-10: F41.1): patients 7 y/o and older, and adults
- **Juvenile Fibromyalgia Syndrome** (ICD-10: M79.7): patients 13 to 17 y/o
- **Fibromyalgia** (ICD-10: M79.7): adults only
- **Major Depressive Disorder** (ICD-10: F32.x, F33.x): **adults only.** Not approved at any pediatric age
- **Diabetic Peripheral Neuropathic Pain** (ICD-10: E11.42 with G63): adults only
- **Chronic Musculoskeletal Pain** (ICD-10: M79.1, G89.29): adults only

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Off-Label Uses

- **Pediatric major depressive disorder** (ICD-10: F32.x, F33.x): specifically negative. Efficacy was not demonstrated in two 10-week trials, 800 patients aged 7 to 17.
- **ADHD** (ICD-10: F90.x): insufficient. No ADHD indication or trial at any age; use an approved non-stimulant (Strattera, Qelbree).
- **Pediatric neuropathic and musculoskeletal pain** (ICD-10: G63, M79.1): insufficient; not established below adulthood.
- **Other pediatric anxiety disorders** (ICD-10: F40.x, F93.0, F41.0): insufficient; the evidence is confined to GAD.

Contraindications & Warnings

- **Boxed Warning:** SUICIDAL THOUGHTS AND BEHAVIORS. Antidepressants increased suicidal thinking and behaviour in children, adolescents and young adults. Monitor closely for worsening and emergent suicidality, particularly in the first months and at every dose change.
- **Contraindicated:**
  - Concomitant MAOI antidepressant, or use within 14 days of stopping one.
  - Initiation in a patient taking linezolid or intravenous methylene blue.
- **Use with caution, or avoid** (Warnings in this label, not contraindications):
  - Chronic liver disease, cirrhosis or substantial alcohol use: avoid, because of fatal hepatic failure.
  - Severe renal impairment with GFR under 30 mL/min: avoid.
  - Untreated anatomically narrow angles: angle-closure glaucoma.
  - Other serotonergic drugs; serotonin syndrome occurs with duloxetine alone.
  - Antiplatelets, anticoagulants and NSAIDs: increased bleeding.
  - History of seizure disorder; such patients were excluded from the trials.
  - Pre-existing hypertension, and any risk of orthostatic hypotension, falls or syncope.
  - Bipolar disorder or risk factors for it: activation of mania.
  - Diabetes, and conditions that slow gastric emptying.
- **Screen before starting:**
  - Personal and family history of bipolar disorder, mania or hypomania.
  - Blood pressure, measured before initiation.
  - Liver history including alcohol use, and renal function.
  - Medication list for MAOIs, serotonergic agents, CYP1A2 inhibitors, antiplatelets.
  - Baseline height and weight, plotted on a growth chart.

Drug Interactions

- **MAOIs** (phenelzine, tranylcypromine, linezolid, intravenous methylene blue): serotonin syndrome. Contraindicated; allow 14 days in either direction.

- **Potent CYP1A2 inhibitors** (fluvoxamine, ciprofloxacin, enoxacin) and thioridazine: avoid. Qelbree is a strong CYP1A2 inhibitor.
- **Potent CYP2D6 inhibitors** (paroxetine, fluoxetine, quinidine, bupropion): duloxetine levels rise. Reduce the dose or choose another agent.
- **CYP2D6 substrates** (antidepressants, antipsychotics, atomoxetine, metoprolol): exposure rises. Reduce the substrate dose.
- **Other serotonergic drugs** (SSRIs, SNRIs, triptans, tramadol, lithium, buspirone, St John's Wort): serotonin syndrome. Reassess within 1 week of any change.
- **NSAIDs, aspirin, warfarin, antiplatelets:** increased bleeding. Reconsider routine NSAID use.
- **Drugs causing hyponatremia** (thiazides, carbamazepine): additive SIADH risk. Check sodium for lethargy or confusion.

Administration

- Give once daily, with or without food; food blunts early nausea.
- Swallow the capsule whole. Do not crush, chew, open or sprinkle it onto food.
- If the patient cannot swallow capsules, prescribe the separate sprinkle product.
- The adult MDD label permits 20 mg twice daily; every pediatric step is once daily.
- Missed dose: take when remembered unless the next is near; do not double up.
- Never stop abruptly. See Discontinuation & Taper.

Side Effects

- **Common** (pediatric, at least 5% and twice placebo): decreased weight and appetite, nausea, vomiting, diarrhea, dizziness, fatigue
- **Serious:**
  - Suicidal thoughts and behaviour: the boxed warning.
  - Hepatotoxicity including fatal hepatic failure: discontinue for jaundice or liver dysfunction.
  - Serotonin syndrome: stop all serotonergic agents and treat as an emergency.
  - Erythema multiforme and Stevens-Johnson syndrome: stop at first blistering or mucosal erosion.
  - Increased bleeding; mania or hypomania; seizures.
  - Angle-closure glaucoma: sudden eye pain or visual change needs same-day ophthalmology.
  - Hyponatremia with SIADH; orthostatic hypotension, falls and syncope; raised blood pressure.
  - Discontinuation syndrome: dizziness, headache, nausea, electric-shock paresthesia, irritability, insomnia, anxiety.

    - Growth effect: mean 0.1 kg loss at 10 weeks against 0.9 kg gain on placebo; mean height percentile fell 1% over 9 months.

Monitoring & Labs

- **Suicidality:** weekly for 4 weeks, every visit through 3 months, every dose change, then each routine visit.
- **Blood pressure:** baseline, 4 weeks, every dose change, then every 3 months. Include a standing reading.
- **Growth:** height and weight on a growth chart at baseline, then every 3 months. Investigate a 3.5% weight loss.
- **Liver:** no routine schedule. Check ALT, AST and bilirubin for jaundice or right upper quadrant pain; ask about alcohol each visit.
- **Sodium:** not routine. Check for headache, confusion or unsteadiness; at 2 to 4 weeks if on a thiazide or carbamazepine.
- **Bleeding and psychiatric:** ask about bruising, nosebleeds and mania each visit during titration, then every 3 months.
- **Glucose:** in diabetes, check A1c 3 months after starting; not routine otherwise.

Discontinuation & Taper

- Do not stop abruptly; the label directs gradual dose reduction.
- Symptoms follow tapered as well as abrupt cessation: dizziness, headache, nausea, paresthesia, irritability, insomnia, anxiety.
- If intolerable symptoms follow a reduction, resume the previous dose and decrease more gradually.
- Drug holidays are not appropriate; a missed weekend causes discontinuation symptoms.
- Discontinue immediately for jaundice, serotonin syndrome, or a serious skin reaction.

Pregnancy & Lactation

- **Pregnancy:** no clear risk of major birth defects. Use in the month before delivery may increase postpartum haemorrhage.
    - Third-trimester SNRI exposure may cause neonatal poor adaptation: respiratory distress, feeding difficulty, hypotonia, tremor, irritability.
    - Background risk is 2 to 4% for birth defects, 15 to 20% for miscarriage; weigh continuation against relapse.
- **Lactation:** milk and infant serum levels are low; not a reason to stop breastfeeding. Prefer a better-studied agent for a newborn or preterm infant. Galactorrhea reported in

mothers. (LactMed 2024)
- **Exposure Registry:** National Pregnancy Registry for Antidepressants, 1-866-961-2388, womensmentalhealth.org

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Counseling Points

- **Counsel the family on:**
  - Never running out; missed doses cause dizziness and electric-shock sensations.
  - Holding the starting dose a full 2 weeks in anxiety before any increase.
  - Nausea in the first week or two, usually settled by food.
  - Swallowing the capsule whole, never opening it onto food.
  - Avoiding alcohol as a liver instruction, and asking before any NSAID.
  - Daily observation for new agitation or talk of self-harm through the first months.
- **Advise them to call for:**
  - New or worsening talk of self-harm, or a sudden change in mood.
  - Yellowing of the skin or eyes, dark urine, or pain under the right ribs.
  - Shivering with twitching, agitation, fever and a racing heart.
  - A rash with blisters, peeling skin, or sores in the mouth or eyes.
  - Unusual bruising, persistent nosebleeds, or bleeding gums.
  - Headache with confusion, unsteadiness or unusual sleepiness.
  - Sudden eye pain, redness or blurred vision, or fainting on standing.

References

1. DailyMed. Cymbalta (duloxetine delayed-release capsules) prescribing information. 2023. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=2f7d4d67-10c1-4bf4-a7f2-c185fbad64ba
2. LactMed. Duloxetine. Drugs and Lactation Database, National Institute of Child Health and Human Development. 2024. https://www.ncbi.nlm.nih.gov/books/NBK501470/
3. FDA. National Drug Code Directory, openFDA. Queried by generic name duloxetine. 2026. https://api.fda.gov/drug/ndc.json?search=generic_name:%22duloxetine%22&limit=1000

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