

FLUoxetine (Lexi-Drugs)
ALERT: U.S. Boxed Warning

The FDA-approved labeling includes a boxed warning. See Warnings/Precautions section for a concise summary of this information. For verbatim wording of the boxed warning, consult the product labeling or www.fda.gov.

Special Alerts

SSRI Use During Pregnancy and Potential Risk of Persistent Pulmonary Hypertension of the Newborn (PPHN) December 2011

Pronunciation

(floo OKS e teen)

Brand Names: U.S.

PROzac®; PROzac® Weekly™; Sarafem®

Brand Names: Canada

Apo-Fluoxetine®; Ava-Fluoxetine; CO Fluoxetine; Dom-Fluoxetine; Fluoxetine Capsules BP; FXT 40; Gen-Fluoxetine; JAMP-Fluoxetine; Mint-Fluoxetine; Mylan-Fluoxetine; Novo-Fluoxetine; Nu-Fluoxetine; PHL-Fluoxetine; PMS-Fluoxetine; PRO-Fluoxetine; Prozac®; Q-Fluoxetine; ratio-Fluoxetine; Riva-Fluoxetine; Sandoz-Fluoxetine; Teva-Fluoxetine; ZYM-Fluoxetine

Dosing: Pediatric

Depression: Oral: 8-18 years: 10-20 mg/day; lower-weight children can be started at 10 mg/day, may increase to 20 mg/day after 1 week if needed

Obsessive-compulsive disorder: Oral: 7-17 years: Initial: 10 mg/day; may increase after 2 weeks if inadequate clinical response to 20 mg/day; further increases may be considered after several weeks to recommended range of 20-30 mg/day (lower weight children) or 20-60 mg/day (adolescents and higher weight children)

Selective mutism (unlabeled use): Oral: 5-18 years: Initial: 5-10 mg/day; titrate upwards as needed (usual maximum dose: 60 mg/day)

Note: Upon discontinuation of fluoxetine therapy, gradually taper dose. If intolerable symptoms occur following a dose reduction, consider resuming the previously prescribed dose and/or decrease dose at a more gradual rate.

Warnings/Precautions

Boxed Warnings:

- Suicidal thinking/behavior: See “Major psychiatric warnings” below.

Major psychiatric warnings:

- Suicidal thinking/behavior: **[U.S. Boxed Warning]: Antidepressants increase the risk of suicidal thinking and behavior in children, adolescents, and young adults (18-24 years of age) with**

major depressive disorder (MDD) and other psychiatric disorders; consider risk prior to prescribing. Short-term studies did not show an increased risk in patients >24 years of age and showed a decreased risk in patients ≥65 years. Closely monitor patients for clinical worsening, suicidality, or unusual changes in behavior, particularly during the initial 1-2 months of therapy or during periods of dosage adjustments (increases or decreases); the patient's family or caregiver should be instructed to closely observe the patient and communicate condition with healthcare provider. A medication guide concerning the use of antidepressants should be dispensed with each prescription. **Fluoxetine is FDA approved for the treatment of OCD in children ≥7 years of age and MDD in children ≥8 years of age.**

- The possibility of a suicide attempt is inherent in major depression and may persist until remission occurs. Patients treated with antidepressants should be observed for clinical worsening and suicidality, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases. Worsening depression and severe abrupt suicidality that are not part of the presenting symptoms may require discontinuation or modification of drug therapy. Use caution in high-risk patients during initiation of therapy.
- Prescriptions should be written for the smallest quantity consistent with good patient care. The patient's family or caregiver should be alerted to monitor patients for the emergence of suicidality and associated behaviors such as anxiety, agitation, panic attacks, insomnia, irritability, hostility, impulsivity, akathisia, hypomania, and mania; patients should be instructed to notify their healthcare provider if any of these symptoms or worsening depression or psychosis occur.

Concerns related to adverse effects:

- Allergic events and rash: Fluoxetine use has been associated with occurrences of significant rash and allergic events, including vasculitis, lupus-like syndrome, laryngospasm, anaphylactoid reactions, and pulmonary inflammatory disease. Discontinue if underlying cause of rash cannot be identified.
- Anticholinergic effects: Relatively devoid of these side effects
- Bleeding risk: May impair platelet aggregation resulting in increased risk of bleeding events, particularly if used concomitantly with aspirin, NSAIDs, warfarin or other anticoagulants. Bleeding related to SSRI use has been reported to range from relatively minor bruising and epistaxis to life-threatening hemorrhage.
- CNS depression: Has a low potential to impair cognitive or motor performance; caution operating hazardous machinery or driving.
- CNS effects: May cause insomnia, anxiety, nervousness, or anorexia.
- Neuroleptic malignant syndrome (NMS): Use may be associated with NMS; monitor for mental status changes, fever, muscle rigidity, and/or autonomic instability.
- Serotonin syndrome (SS)/neuroleptic malignant syndrome (NMS)-like reactions: SS and NMS-like reactions have occurred with serotonin/norepinephrine reuptake inhibitors (SNRIs) and selective serotonin reuptake inhibitors (SSRIs) when used alone, and particularly when used in combination with serotonergic agents (eg, triptans) or antidopaminergic agents (eg, antipsychotics). The diagnosis of SS can be made using the Hunter Serotonin Toxicity Criteria (Dunkley, 2003). Identification and differentiation of SS (eg, tremor, myoclonus, agitation) and more severe NMS-like reactions (eg, hyperthermia, muscle rigidity, autonomic instability,

mental status changes) can be complex; monitor patients closely for either syndrome. Discontinue treatment (and any concomitant serotonergic and/or antidopaminergic agents) immediately if signs/symptoms arise.

- Sexual dysfunction: May cause or exacerbate sexual dysfunction.
- SIADH and hyponatremia: SSRIs and SNRIs have been associated with the development of SIADH; hyponatremia has been reported rarely (including severe cases with serum sodium <110 mmol/L), predominately in the elderly. Volume depletion and/or concurrent use of diuretics likely increases risk.
- Weight loss: May cause anorexia and/or weight loss. Use caution in patients where weight loss is undesirable.

Disease-related concerns:

- Cardiovascular disease: Use with caution in patients with a history of MI or unstable heart disease; experience in these patients is limited.
- Diabetes: Use with caution in patients with diabetes mellitus; may alter glycemic control and may require adjustment of antidiabetic medication; hypoglycemia and hyperglycemia has been observed during and after cessation of therapy, respectively.
- Hepatic impairment: Use with caution in patients with hepatic impairment; clearance is decreased and plasma concentrations are increased; a lower dosage may be needed in patients with cirrhosis.
- Mania/hypomania: May worsen psychosis in some patients or precipitate a shift to mania or hypomania in patients with bipolar disorder. Monotherapy in patients with bipolar disorder should be avoided. Patients presenting with depressive symptoms should be screened for bipolar disorder. **Fluoxetine monotherapy is not FDA approved for the treatment of bipolar depression.** Safety and efficacy in children <8 years of age (major depressive disorder) and <7 years of age (OCD) have not been established.
- Ocular effects: May cause mydriasis; use caution in patients at risk of acute narrow-angle glaucoma or with increased intraocular pressure
- Renal impairment: Use with caution in patients with severe renal impairment; a lower dosage or less frequent dosing may be needed.
- Seizure disorders: Use with caution in patients with a previous seizure disorder or conditions predisposing to seizures such as brain damage or alcoholism.

Concurrent drug therapy issues:

- Agents which lower seizure threshold: Use caution with concurrent therapy.
- Anticoagulants/Antiplatelets: Use caution with concomitant use of NSAIDs, ASA, or other drugs that affect coagulation; the risk of bleeding may be potentiated.
- CNS depressants: Use caution with concomitant therapy.

- MAO inhibitors: Potential for severe reaction when used with MAO inhibitors; autonomic instability, coma, death, delirium, diaphoresis, hyperthermia, mental status changes/agitation, muscular rigidity, myoclonus, neuroleptic malignant syndrome features, and seizures may occur. Concurrent use is contraindicated.
- Proserotonergic agents: Symptoms of agitation, confusion, hallucinations, hyper-reflexia, myoclonus, shivering, and tachycardia may occur with concomitant proserotonergic drugs (ie, SSRIs/SNRIs or triptans), agents which reduce fluoxetine's metabolism, or antidopaminergic agents (including antipsychotics). Concurrent use of serotonin precursors (eg, tryptophan) is not recommended.
- Thioridazine or pimozide: Fluoxetine may elevate plasma levels of these drugs, increasing risk of QT_c interval prolongation; this may lead to serious ventricular arrhythmias, such as torsade de pointes-type arrhythmias, and sudden death. **Concurrent use is contraindicated.**

Special populations:

- Elderly: Use caution in elderly patients; may cause or exacerbate syndrome of inappropriate antidiuretic hormone secretion or hyponatremia; monitor sodium closely with initiation or dosage adjustments in older adults (Beers Criteria). May also cause agitation, sleep disturbances, and excessive CNS stimulation.

Other warnings/precautions:

- Electroconvulsive therapy: May increase the risks associated with electroconvulsive therapy; consider discontinuing, when possible, prior to ECT treatment.
- Long half-life: Due to the long half-life of fluoxetine and its metabolites, the effects and interactions noted may persist for prolonged periods following discontinuation.
- Withdrawal syndrome: May cause dysphoric mood, irritability, agitation, dizziness, sensory disturbances (eg, electric shock-like sensations), anxiety, confusion, headache, lethargy, emotional lability, insomnia, hypomania, tinnitus, and seizures. Upon discontinuation of fluoxetine therapy, gradually taper dose. If intolerable symptoms occur following a decrease in dosage or upon discontinuation of therapy, then resuming the previous dose with a more gradual taper should be considered.