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**LUVOX**

**Dosage Forms & Strengths**

**Obsessive-Compulsive Disorder**

Conventional tablets

* 50 mg qHS initially; may increase by 50 mg/day q4-7Days up to 100-300 mg/day
* Dose >100 mg/day should be divided q12hr

Extended-release capsules

* 100 mg PO qDay initially; may titrate in 50 mg/day increments every week
* Not to exceed 300 mg/day

**Social Phobia (Off-label)**

Immediate release

* 50 mg PO qDay; may increase by 50 mg at 1 week interval; usual dose range is 100-300 mg/day

Extended-release capsules

* 100 mg PO qDay initially; may titrate in 50 mg/day increments qWeek
* Not to exceed 300 mg/day

**Panic Disorder (Off-label)**

50 mg PO qDay; after several days, gradually increase to 150 mg/day; may increase to 300 mg/day for patients who fail to respond after several weeks of treatment

Dosing considerations

* Continue therapy for 1-2 years, and consider discontinuation with close supervision; when discontinuing therapy, a slow taper over 2-6 months is recommended

**Posttraumatic Stress Disorder (Off-label)**

50 mg/day PO initially; may increase dose to 100-250 mg in adults and 100 mg in older adults; not to exceed 300 mg/day

Dosing considerations

* Patients who respond to therapy may need to continue therapy indefinitely
* May attempt tapering after 6-12 months in patients with acute PTSD; tapering should occur gradually over 2 weeks to 1 month to avoid withdrawal symptoms; tapering should take place over 4-12 weeks in patients at risk of relapse

**Dosing Modifications**

Hepatic impairment: Decrease dose

## Pharmacology

### Mechanism of Action

Selective serotonin reuptake inhibitor; little or no affinity for dopamine, alpha-adrenergic histamine, or cholinergic receptor

### Absorption

Bioavailability: 53%

Peak plasma time: 3-8 hr

Peak plasma concentration: 88-546 ng/mL (nonlinear)

### Distribution

Protein bound: 80%

Vd: 25 L/kg

### Metabolism

Metabolism: Hepatic oxidative demethylation, deamination

Metabolites: Inactive

Enzymes inhibited: Hepatic CYP1A2, CYP2C9, CYP3A4

### Elimination

Half-life: 15.6 hr; 17.4-25.9 hr (elderly)

Dialyzable: No

Excretion: Urine (85%)

### Pharmacogenomics

Several SSRIs (eg, fluoxetine, fluvoxamine, paroxetine, sertraline) are metabolized by CYP2D6

CYP2D6 is involved in the metabolism of approximately 20% of drugs in clinical use and displays large individual-to-individual variability in activity due to genetic polymorphisms

More than 80 CYP2D6 variant alleles have been identified; however, 4 of the most prevalent alleles, CYP2D6\*3, \*4, \*5, and \*6, account for 93-97% of CYP2D6 poor metabolizers (PMs)

CYP2D6\*4, the most common variant (~25% frequency in whites), causes a splicing defect; CYP2D6\*3 (2.7% frequency) causes a frameshift mutation; and CYP3D6\*5 (2.6%) is an entire deletion of the CYP2D6 gene; individuals homozygous for these alleles have no CYP2D6 activity

The impact of CYP2D6 activity is further complicated in some SSRIs (eg, fluoxetine, fluvoxamine, paroxetine, sertraline) that, in addition to being substrates for CYP2D6, are also known to moderately inhibit CYP2D6 activity

Interactions

**Contraindicated (12)**

* alosetron
* astemizole
* cisapride
* isocarboxazid
* phenelzine
* pimozide
* procarbazine
* ramelteon
* selegiline
* terfenadine
* thioridazine
* tranylcypromine

**Serious - Use Alternative (105)**

* alfentanil
* almotriptan
* alosetron
* amiodarone
* amitriptyline
* amoxapine
* apixaban
* arsenic trioxide
* astemizole
* bupropion
* buspirone
* cilostazol
* cimetidine
* cisapride
* citalopram
* clomipramine
* clopidogrel
* clozapine
* cyclobenzaprine
* cyclosporine
* desipramine
* desvenlafaxine
* dextromethorphan
* dihydroergotamine
* dihydroergotamine intranasal
* disopyramide
* dolasetron
* dosulepin
* doxepin
* dronedarone
* duloxetine
* dyphylline
* eltrombopag
* ergotamine
* escitalopram
* esomeprazole
* etravirine
* everolimus
* fentanyl
* fentanyl intranasal
* fentanyl iontophoretic transdermal system
* fentanyl transdermal
* fentanyl transmucosal
* fluoxetine
* granisetron
* hydromorphone
* ibutilide
* imipramine
* indapamide
* levobupivacaine
* levomilnacipran
* lidocaine
* linezolid
* lofepramine
* lorcaserin
* lovastatin
* maprotiline
* meperidine
* methylene blue
* metoclopramide
* mexiletine
* mianserin
* milnacipran
* morphine
* nefazodone
* netupitant/palonosetron
* nortriptyline
* olanzapine
* omeprazole
* ondansetron
* palonosetron
* paroxetine
* pazopanib
* pentamidine
* phentermine
* pimozide
* pirfenidone
* pomalidomide
* procainamide
* protriptyline
* quinidine
* ramelteon
* ranolazine
* rasagiline
* remifentanil
* ropinirole
* selegiline transdermal
* sertindole
* sertraline
* sotalol
* st john's wort
* sufentanil
* sufentanil sl
* tedizolid
* terfenadine
* theophylline
* tipranavir
* tizanidine
* tolvaptan
* trazodone
* trimipramine
* venlafaxine
* vilazodone
* vortioxetine
* warfarin

## Warnings

### Black Box Warnings

In short-term studies, antidepressants increased the risk of suicidal thinking and behavior in children, adolescents, and young adults (<24 years) taking antidepressants for major depressive disorders and other psychiatric illnesses

This increase was not seen in patients aged >24 years; a slight decrease in suicidal thinking was seen in adults >65 years

In children and young adults, risks must be weighed against the benefits of taking antidepressants

Patients should be monitored closely for changes in behavior, clinical worsening, and suicidal tendencies; this should be done during initial 1-2 months of therapy and dosage adjustments

The patient’s family should communicate any abrupt changes in behavior to the healthcare provider

Worsening behavior and suicidal tendencies that are not part of the presenting symptoms may require discontinuation of therapy

This drug is not approved for use in pediatric patients

### Contraindications

Hypersensitivity

Coadministration with serotonergic drugs

* Concomitant use or within 14 days of MAOIs increases risk of serotonin syndrome
* Reactions to concomitant administration with MAOIs include tremor, myoclonus, diaphoresis, nausea, vomiting, flushing, dizziness, hyperthermia with features resembling neuroleptic malignant syndrome, seizures, rigidity, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes (including extreme agitation progressing to delirium and coma)
* Starting fluvoxamine in a patient who is being treated with linezolid or IV methylene blue is contraindicated because of an increased risk of serotonin syndrome
* If linezolid or IV methylene blue must be administered, discontinue SSRI immediately and monitor for CNS toxicity; may resume 24 hr after last linezolid or methylene blue dose, or after 2 weeks of monitoring (5 weeks for fluoxetine), whichever comes first

### Cautions

Conflicting evidence regarding use of SSRIs during pregnancy and increased risk of persistent pulmonary hypertension of the newborn (see Pregnancy)

In neonates exposed to SNRIs/SSRIs late in third trimester: Risk of complications such as feeding difficulties, irritability, and respiratory problems

Risk of mydriasis; may trigger angle closure attack in patients with angle closure glaucoma with anatomically narrow angles without a patent iridectomy

May need to modify dose for hepatic impairment; titrate at smaller increments and longer intervals

Clinical worsening and suicide ideation may occur despite medication in adolescents and young adults (18-24 years)

May worsen mania symptoms or precipitate mania in patients with bipolar disorder

Increases risk of bleeding in patients taking anticoagulants/antiplatelets concomitantly

Do not use concurrently with alosetron, astemizole, cisapride, pimozide, terfenadine, or tizanidine due to QT prolongation risk

Potentially life-threatening serotonin syndrome reported when coadministered with drugs that impair serotonin metabolism (in particular, MAOIs, including nonpsychiatric MAOIs, such as linezolid and IV methylene blue) (see Contraindications)

May impair ability to operate heavy machinery and other tasks requiring mental alertness

Bone fractures have been associated with antidepressant treatment; consider possibility of fragility fracture if patient presents with pain, joint tenderness, or swelling

Impaired glucose control (hyperglycemia or hypoglycemia) reported; monitor for signs/symptoms of loss of glucose control, especially in patients with diabetes

May cause or exacerbate sexual dysfunction

Syndrome of inapropriate antidiuretic hormone and hyponatremia reported with SSRI and SNRI use; volume deplretion and/or concurrent use of diuretics may increase risk; consider discontinuing therapy if symptomatic hyponatremia occurs

Use caution in patients with cardiovascular disease or history of seizure disorder