**THERAPEUTICS**

**Brands** • Lexapro  
*see index for additional brand names*

**Generic?** Yes

**Class**
- Neuroscience-based Nomenclature: serotonin reuptake inhibitor (S-RI)  
- SSRI (selective serotonin reuptake inhibitor); often classified as an antidepressant, but it is not just an antidepressant

**Commonly Prescribed for**  
(bold for FDA approved)
- Major depressive disorder (ages 12 and older)  
- Generalized anxiety disorder (GAD)  
- Panic disorder  
- Obsessive-compulsive disorder (OCD)  
- Posttraumatic stress disorder (PTSD)  
- Social anxiety disorder (social phobia)  
- Premenstrual dysphoric disorder (PMDD)

**How the Drug Works**
- Boosts neurotransmitter serotonin  
- Blocks serotonin reuptake pump (serotonin transporter)  
- Desensitizes serotonin receptors, especially serotonin 1A autoreceptors  
- Presumably increases serotonergic neurotransmission

**How Long Until It Works**
- Onset of therapeutic actions usually not immediate, but often delayed 2–4 weeks  
- If it is not working within 6–8 weeks, it may require a dosage increase or it may not work at all  
- May continue to work for many years to prevent relapse of symptoms

**If It Works**
- The goal of treatment is complete remission of current symptoms as well as prevention of future relapses  
- Treatment most often reduces or even eliminates symptoms, but not a cure since symptoms can recur after medicine stopped  
- Continue treatment until all symptoms are gone (remission) or significantly reduced (e.g., OCD, PTSD)

**If It Doesn’t Work**
- Many patients have only a partial response where some symptoms are improved but others persist (especially insomnia, fatigue, and problems concentrating in depression)  
- Other patients may be nonresponders, sometimes called treatment-resistant or treatment-refractory  
- Some patients who have an initial response may relapse even though they continue treatment, sometimes called “poop-out”  
- Consider increasing dose, switching to another agent or adding an appropriate augmenting agent  
- Consider psychotherapy  
- Consider evaluation for another diagnosis or for a comorbid condition (e.g., medical illness, substance abuse, etc.)  
- Some patients may experience apparent lack of consistent efficacy due to activation of latent or underlying bipolar disorder, and require antidepressant discontinuation and a switch to a mood stabilizer

**Best Augmenting Combos for Partial Response or Treatment Resistance**
- Trazodone, especially for insomnia  
- Bupropion, mirtazapine, reboxetine, or atomoxetine (use combinations of antidepressants with caution as this may activate bipolar disorder and suicidal ideation)  
- Modafinil, especially for fatigue, sleepiness, and lack of concentration  
- Mood stabilizers or atypical antipsychotics for bipolar depression, psychotic depression, treatment-resistant depression, or treatment-resistant anxiety disorders  
- Benzodiazepines  
- If all else fails for anxiety disorders, consider gabapentin or tiagabine  
- Hypnotics for insomnia  
- Classically, lithium, buspirone, or thyroid hormone
Rare activation of suicidal ideation and behavior (suicidality) (short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo beyond age 24)

Weight Gain
- Reported but not expected

Sedation
- Reported but not expected

What to Do About Side Effects
- Wait
- Wait
- Wait
- In a few weeks, switch to another agent or add other drugs

Best Augmenting Agents for Side Effects
- Often best to try another SSRI or another antidepressant monotherapy prior to resorting to augmentation strategies to treat side effects
- Trazodone or a hypnotic for insomnia
- Bupropion, sildenafil, vardenafil, or tadalafil for sexual dysfunction
- Bupropion for emotional flattening, cognitive slowing, or apathy
- Mirtazapine for insomnia, agitation, and gastrointestinal side effects
- Benzodiazepines for jitteriness and anxiety, especially at initiation of treatment and especially for anxious patients
- Many side effects are dose-dependent (i.e., they increase as dose increases, or they reemerge until tolerance redevelops)
- Many side effects are time-dependent (i.e., they start immediately upon dosing and upon each dose increase, but go away with time)
- Activation and agitation may represent the induction of a bipolar state, especially a mixed dysphoric bipolar II condition sometimes associated with suicidal ideation, and require the addition of lithium, a mood stabilizer or an atypical antipsychotic, and/or discontinuation of escitalopram

Notable Side Effects
- Sexual dysfunction (men: delayed ejaculation, erectile dysfunction; men and women: decreased sexual desire, anorgasmia)
- Gastrointestinal (decreased appetite, nausea, diarrhea, constipation, dry mouth)
- Mostly central nervous system (insomnia but also sedation, agitation, tremors, headache, dizziness)
- Note: patients with diagnosed or undiagnosed bipolar or psychotic disorders may be more vulnerable to CNS-activating actions of SSRIs
- Autonomic (sweating)
- Bruising and rare bleeding
- Rare hyponatremia (mostly in elderly patients and generally reversible on discontinuation of escitalopram)
- SIADH (syndrome of inappropriate antidiuretic hormone secretion)

Life-Threatening or Dangerous Side Effects
- Rare seizures
- Rare induction of mania
Many patients tolerate 50% dose reduction for 3 days, then another 50% reduction for 3 days, then discontinuation. If withdrawal symptoms emerge during discontinuation, raise dose to stop symptoms and then restart withdrawal much more slowly.

Pharmacokinetics
- Mean terminal half-life 27–32 hours
- Steady-state plasma concentrations achieved within 1 week
- No significant actions on CYP450 enzymes

Drug Interactions
- Tramadol increases the risk of seizures in patients taking an antidepressant
- Can cause a fatal “serotonin syndrome” when combined with MAOIs, so do not use with MAOIs or for at least 14 days after MAOIs are stopped
- Do not start an MAOI for at least 5 half-lives (5 to 7 days for most drugs) after discontinuing escitalopram
- Could theoretically cause weakness, hyperreflexia, and incoordination when combined with sumatriptan or possibly other triptans, requiring careful monitoring of patient
- Possible increased risk of bleeding, especially when combined with anticoagulants (e.g., warfarin, NSAIDs)
- NSAIDs may impair effectiveness of SSRIs
- Few known adverse drug interactions

Other Warnings/Precautions
- Use with caution in patients with history of seizures
- Use with caution in patients with bipolar disorder unless treated with concomitant mood-stabilizing agent
- When treating children, carefully weigh the risks and benefits of pharmacological treatment against the risks and benefits of nontreatment with antidepressants and make sure to document this in the patient’s chart
- Distribute the brochures provided by the FDA and the drug companies

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**Dosing and Use**

**Usual Dosage Range**
- 10–20 mg/day

**Dosage Forms**
- Tablets 5 mg, 10 mg (scored), 20 mg (scored)
- Capsule 5 mg, 10 mg, 20 mg
- Oral solution 5 mg/5 mL

**How to Dose**
- Initial 10 mg/day; increase to 20 mg/day if necessary; single dose administration, morning or evening

**Dosing Tips**
- Given once daily, any time of day tolerated
- 10 mg of escitalopram may be comparable in efficacy to 40 mg of citalopram with fewer side effects
- Thus, give an adequate trial of 10 mg prior to giving 20 mg
- Some patients require dosing with 30 or 40 mg
- If intolerable anxiety, insomnia, agitation, akathisia, or activation occur either upon dosing initiation or discontinuation, consider the possibility of activated bipolar disorder and switch to a mood stabilizer or an atypical antipsychotic

**Overdose**
- Few reports of escitalopram overdose, but probably similar to citalopram overdose
- Rare fatalities have been reported in citalopram overdose, both in combination with other drugs and alone
- Symptoms associated with citalopram overdose include vomiting, sedation, heart rhythm disturbances, dizziness, sweating, nausea, tremor, and rarely amnesia, confusion, coma, convulsions

**Long-Term Use**
- Safe

**Habit Forming**
- No

**How to Stop**
- Taper not usually necessary
- However, tapering to avoid potential withdrawal reactions generally prudent

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**How to Stop**
- Taper not usually necessary
- However, tapering to avoid potential withdrawal reactions generally prudent
• Warn patients and their caregivers about the possibility of activating side effects and advise them to report such symptoms immediately
• Monitor patients for activation of suicidal ideation, especially children and adolescents

Do Not Use
• If patient is taking an MAOI
• If patient is taking pimozide
• If there is a proven allergy to escitalopram or citalopram

Pregnancy
• Effective June 30, 2015, the US FDA requires changes to the content and format of pregnancy and lactation information in prescription drug labels, including the elimination of the pregnancy letter categories; the Pregnancy and Lactation Labeling Rule (PLLR or final rule) applies only to prescription drugs and will be phased in gradually for drugs approved on or after June 30, 2001
• Controlled studies have not been conducted in pregnant women
• Not generally recommended for use during pregnancy, especially during first trimester
• Nonetheless, continuous treatment during pregnancy may be necessary and has not been proven to be harmful to the fetus
• At delivery there may be more bleeding in the mother and transient irritability or sedation in the newborn
• Must weigh the risk of treatment (first trimester fetal development, third trimester newborn delivery) to the child against the risk of no treatment (recurrence of depression, maternal health, infant bonding) to the mother and child
• For many patients, this may mean continuing treatment during pregnancy
• Exposure to SSRIs early in pregnancy may be associated with increased risk of septal heart defects (absolute risk is small)
• SSRI use beyond the 20th week of pregnancy may be associated with increased risk of pulmonary hypertension in newborns, although this is not proven
• Exposure to SSRIs late in pregnancy may be associated with increased risk of gestational hypertension and preeclampsia
• Neonates exposed to SSRIs or SNRIs late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support,

SPECIAL POPULATIONS

Renal Impairment
• No dose adjustment for mild to moderate impairment
• Use cautiously in patients with severe impairment

Hepatic Impairment
• Recommended dose 10 mg/day

Cardiac Impairment
• Not systematically evaluated in patients with cardiac impairment
• Preliminary data suggest that citalopram is safe in patients with cardiac impairment, suggesting that escitalopram is also safe
• Treating depression with SSRIs in patients with acute angina or following myocardial infarction may reduce cardiac events and improve survival as well as mood

Elderly
• Recommended dose 10 mg/day
• Risk of SIADH with SSRIs is higher in the elderly
• Reduction in the risk of suicidality with antidepressants compared to placebo in adults age 65 and older

Children and Adolescents
• Approved for depression in adolescents ages 12–17
• Carefully weigh the risks and benefits of pharmacological treatment against the risks and benefits of nontreatment with antidepressants and make sure to document this in the patient’s chart
and tube feeding; reported symptoms are consistent with either a direct toxic effect of SSRIs and SNRIs or, possibly, a drug discontinuation syndrome, and include respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying.

Pearls

✽ May be among the best-tolerated antidepressants
✽ May have less sexual dysfunction than some other SSRIs
✽ May be better tolerated than citalopram
✽ Can cause cognitive and affective “flattening”
✽ R-citalopram may interfere with the binding of S-citalopram at the serotonin transporter
✽ For this reason, S-citalopram may be more than twice as potent as R,S-citalopram (i.e., citalopram)
✽ Thus, 10 mg starting dose of S-citalopram may have the therapeutic efficacy of 40 mg of R,S-citalopram
✽ Thus, escitalopram may have faster onset and better efficacy with reduced side effects compared to R,S-citalopram
✽ Some data may actually suggest remission rates comparable to SNRIs, but this is not proven

✽ Escitalopram is commonly used with augmenting agents, as it is the SSRI with the least interaction at either CYP450 2D6 or 3A4, therefore causing fewer pharmacokinetically mediated drug interactions with augmenting agents than other SSRIs
✽ SSRIs may be less effective in women over 50, especially if they are not taking estrogen
✽ SSRIs may be useful for hot flushes in perimenopausal women
✽ Some postmenopausal women’s depression will respond better to escitalopram plus estrogen augmentation than to escitalopram alone
✽ Nonresponse to escitalopram in elderly may require consideration of mild cognitive impairment or Alzheimer disease

THE ART OF PSYCHOPHARMACOLOGY

Potential Advantages
• Patients taking concomitant medications (few drug interactions and fewer even than with citalopram)
• Patients requiring faster onset of action

Potential Disadvantages
• More expensive than citalopram in markets where citalopram is generic

Primary Target Symptoms
• Depressed mood
• Anxiety

Breast Feeding
• Some drug is found in mother’s breast milk
• Trace amounts may be present in nursing children whose mothers are on escitalopram
• If child becomes irritable or sedated, breast feeding or drug may need to be discontinued
• Immediate postpartum period is a high-risk time for depression, especially in women who have had prior depressive episodes, so drug may need to be reinstituted late in the third trimester or shortly after childbirth to prevent a recurrence during the postpartum period
• Must weigh benefits of breast feeding with risks and benefits of antidepressant treatment versus nontreatment to both the infant and the mother
• For many patients, this may mean continuing treatment during breast feeding

• Panic attacks, avoidant behavior, re-experiencing, hyperarousal
• Sleep disturbance, both insomnia and hypersomnia
Suggested Reading

