

SSRI (Selective Serotonin Reuptake Inhibitor)

Tips for Primary Care Providers

Most antidepressants take 3-6 weeks to begin taking effect and up to 6-8 weeks for the full effect. Consider SSRIs when depression, or anxiety disorder is moderate to severe, interferes with daily activities of living, participation in psychotherapy, or when patient has limited improvement despite engaging in psychotherapy.

Titration Tips:

- Start with fluoxetine (Prozac), escitalopram (Lexapro) or sertraline (Zoloft)
- Start at a low dose and increase every 4 weeks.
- Follow-up every 2-4 weeks while titrating the dose.
- If good benefit, continue at minimal effective dose. If no or partial benefit and no significant side effects, continue increasing to max dose.
- If significant side effects develop or there's a lack of benefit at max dose, try second SSRI.
- If good benefit and no significant side effects, continue for a year and then try discontinuing by gradually tapering off the medication. Restart if they relapse.

SSRI	Starting dose (mg)	Titration dose (mg)	FDA Max dose (mg)	Properties	FDA Approval
Fluoxetine (Prozac)	5-10 mg	10 mg	60 mg	Long half-life: 5-7 days Less withdrawal symptoms Can be activating Good if medication adherence of concern	MDD (age ≥ 8) OCD (age ≥ 7)
Escitalopram (Lexapro)	5 mg	5 mg	20 mg	Less side effects	MDD (age ≥ 12)
Sertraline (Zoloft)	12.5 mg (age <12) 25 mg (age ≥ 12)	12.5-25 mg (age <12) 25-50 mg (age ≥ 12)	200 mg	Can be slightly sedating Less side effects	OCD (age ≥ 6)

SSRI Side Effects and Management strategies

If side effects occur, they are most notable during the initial 4 weeks of titrating the dose.

Mild & Common Side effects (~10%)	Management strategies
GI upset (Nausea, diarrhea, pain)	<ul style="list-style-type: none"> ▪ Take with food ▪ Usually subsides within 2 weeks
Headache	<ul style="list-style-type: none"> ▪ Supportive care ▪ Usually subsides within 1-2 weeks
Fatigue, low energy	<ul style="list-style-type: none"> ▪ Administer at bedtime ▪ If symptoms persist and impairing, consider switching to different medication.
Difficulty sleeping	<ul style="list-style-type: none"> ▪ Administer in AM ▪ Discuss sleep hygiene, evaluate for other causes of sleep disorders
Less Common Side effects (<10%)	
↑ Agitation, Restlessness Anxiety	<ul style="list-style-type: none"> ▪ Usually self-limiting within 2-4 weeks <p>If persistent and intolerable:</p> <ul style="list-style-type: none"> ▪ Decrease to lower dose ▪ Switch to different medication
Sexual dysfunction	<ul style="list-style-type: none"> ▪ Switch to different medication
Dry mouth	<ul style="list-style-type: none"> ▪ Supportive care (sugarless gum, candy, hydrate)
Tremors	<ul style="list-style-type: none"> ▪ If persists for longer than few weeks, and impairing switch to different medication
Rare & Uncommon Side effects (<1%)	
<p>Black Box Warning</p> <p>(↑ suicidal thoughts/behavior, thoughts of self-harm)</p>	<p>Safety Assessment and Evaluation Consult with psychiatrist or mental health provider</p> <ul style="list-style-type: none"> ○ FDA reviewed 24 studies with 9 different SSRIs (4,400 youth) ○ NO suicides in these studies ○ Adverse events of suicidal ideation and/or self-injurious behavior reported in 3.8% of patients on meds vs. 2.2% on placebo ○ No worsening or new suicidal ideation reported in 17/24 studies that inquired about SI
Increase in appetite	<ul style="list-style-type: none"> ▪ Monitor weight, diet
Increased bleeding time	<ul style="list-style-type: none"> ▪ Medical evaluation, switch medication
Photosensitivity, SIADH	
Serotonin Syndrome (Fever, flushing, muscle rigidity, jaw clenching, tremors, vital instability)	<ul style="list-style-type: none"> ▪ Stop medications ▪ Requires emergent medical evaluation (ER)

How to talk to families about Black-box warnings and side effects

Parent: Is my child/teen more likely to hurt and kill themselves being on an antidepressant?

PCP: In 2004, FDA issued a black box warning that now includes all antidepressants based on 24 RCTs, due to the possible increased risk of suicidal thoughts and behaviors in young people up to age 25. There was a slightly increased risk (3.8% vs. 2.2% with placebo) of suicidal ideation and self-injury, however, **no actual increase in suicides found in these studies.**

- *Black-box warning: Increased thoughts of self-harm, suicidal thoughts/behaviors*
 - *FDA reviewed 24 studies with 9 different SSRIs (4,400 youth)*
 - *NO suicides in these studies*
 - *Adverse events of suicidal ideation and/or self-injurious behavior reported in 3.8% of patients on meds vs. 2.2% on placebo*
 - *No worsening or new suicidal ideation reported in 17/24 studies that inquired about SI*

Parent: Does that mean my child/teen would be better off not taking meds?

PCP: After the black box warning was issued by the FDA, primary care providers felt less comfortable prescribing these meds, and as the prescription rate went down, increased trend of child/teen depression and suicide was observed shortly after. Depression is worth treating, and it is important to regularly follow up with me either in person or by phone to share anything about the medication that may be associated with your child/teen doing worse or better. Please feel free to contact me to discuss any concerns, or before you consider stopping medication.

Parent: Why is the antidepressant causing this unwanted effect?

PCP: We believe that the suicidal thoughts and behaviors are still most likely associated with your child/teen's pre-existing depression. In the process of finding the right medication for their depression symptoms, we encourage your child/teen to also consider therapy. **Combining therapy with medication** can be helpful to allow patients and therapists to develop and build coping skills and language to express their thoughts and feelings, including the destructive and harmful ones.

Parent: Will the medication make my child/teen like a "zombie" or change their personality?

PCP: When taking and titrating as prescribed, SSRIs don't change one's personality. Rarely, at higher doses, blunted affect, apathy or "loss of emotions" can occur. Lowering the dose, augmenting with another medication, or switching to a different antidepressant may help.