

Prozac vs Zoloft

Fluoxetine and sertraline at a glance. A one-page companion to the full comparison at psychiatryrx.org/compare/prozac-vs-zoloft/

Both are SSRIs with decades of use behind them. They share the same mechanism, timeline, and core side effects. The biggest practical difference is half-life, which is how long the medication stays active in the body, and it has real day-to-day consequences.

Side by side

	Fluoxetine (Prozac)	Sertraline (Zoloft)
Drug class	SSRI	SSRI
Half-life	Very long, the longest of the SSRIs. Effects and interactions linger for weeks after the last dose	Much shorter
If a dose is missed or stopped	More forgiving. Discontinuation symptoms are milder and less frequent	More noticeable if stopped abruptly, so it needs a more careful taper
Activation	More activating. Early jitteriness or insomnia is more common in the first weeks	Fairly neutral, though it can be mildly activating too
FDA-approved uses	Major depressive disorder, OCD, bulimia nervosa, panic disorder	Major depressive disorder, panic disorder, PTSD, social anxiety disorder, OCD, PMDD
Side effect tendency	More early activation	More associated with loose stools and diarrhea

What may tip the choice

- Trouble remembering doses, or worry about stopping later: fluoxetine is more forgiving because levels fall slowly on their own.
- Low energy and fatigue front and center: fluoxetine's activation can be a small advantage.
- Already wound up, anxious, or sleeping poorly: sertraline's neutral profile may be the easier start.
- An eating disorder in the picture: fluoxetine is the SSRI approved for bulimia nervosa.
- Broad anxiety needs like PTSD or social anxiety: sertraline carries those formal approvals.
- Planning a future switch to certain other medications: fluoxetine's long half-life means longer washout periods, for example around five weeks before an MAOI.

What they share

- Four to six weeks to fuller effect, sometimes eight. Side effects usually arrive before the benefit.
- Nausea, headache, sweating, sexual side effects, and sleep changes are common early and often ease within one to two weeks.
- Both carry the antidepressant boxed warning for people under 25.
- Both are inexpensive generics.

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