Medications for PTSD

First-line SSRIs and SNRIs, prazosin for nightmares, and augmentation. Trauma-focused therapy is the anchor. Reviewed against current guidelines as of June 8, 2026.

Sertraline and paroxetine carry FDA approval for PTSD. Venlafaxine has strong off-label evidence. Trauma-focused psychotherapy (prolonged exposure, CPT, EMDR) is the treatment with the largest effect and is usually the anchor. Benzodiazepines are usually avoided because they can interfere with the extinction learning that PTSD treatment relies on. Companion to the full guide at psychiatryrx.org/guides/medications-for-ptsd/.

First-line options

Drug	Class	Notes
Sertraline	SSRI (FDA-approved)	50 to 200 mg. Higher doses often needed than for depression. Onset 4 to 6 weeks or longer.
Paroxetine	SSRI (FDA-approved)	20 to 60 mg. Similar evidence. Side effect and discontinuation profile makes it less popular first-line.
Fluoxetine	SSRI (off-label)	Reasonable evidence, widely used. Long half-life is forgiving.
Escitalopram	SSRI (off-label)	Used off-label with some data. Simple dosing.
Venlafaxine XR	SNRI (off-label)	75 to 300 mg. Evidence comparable to SSRIs. Often considered alongside for first-line. Watch BP.
Duloxetine	SNRI (off-label)	Reasonable option when chronic pain is part of the picture.
Trauma-focused therapy	Psychotherapy	Prolonged exposure, CPT, or EMDR. Larger effect size than medication. The anchor of care.

Second-line and augmentation

Drug	Class	When to consider
Prazosin	Alpha-1 antagonist	Nightmares and sleep disturbance. Start 1 mg at bedtime, titrate to 5 to 15 mg. Orthostasis. 2018 VA PACT trial negative overall but many respond.
Risperidone	Atypical antipsychotic	SSRI-refractory PTSD, particularly hyperarousal and re-experiencing. Adjunct, not monotherapy.
Quetiapine	Atypical antipsychotic	100 to 400 mg. Smaller trials for sleep and hyperarousal as adjunct.
Mirtazapine	Atypical antidepressant	Small trials. Reasonable adjunct or alternative when SSRIs are not tolerated.
Topiramate	Anticonvulsant	Some data, particularly with comorbid alcohol use disorder.
Trazodone, DORAs	Sleep	Sleep initiation. Suvorexant, lemborexant, or daridorexant are reasonable.

Special considerations

- Benzodiazepines: VA and DoD guidelines specifically recommend against them for PTSD. Short-term, low-dose PRN use for specific situations is the surviving role. Chronic daily use is associated with worse outcomes in some studies.
- Atypical antipsychotic monotherapy: not supported by evidence. Adjunctive use is reasonable for refractory cases.
- Pregnancy: sertraline is the most-studied SSRI. Paroxetine is avoided in the first trimester.
- Older adults: sertraline or escitalopram at lower doses. Prazosin cautiously with orthostasis monitoring. Avoid heavily anticholinergic agents.
- Comorbid SUD: treat both. Naltrexone, acamprosate, or buprenorphine for the SUD; SSRI for the PTSD. Avoid benzodiazepines.
- Comorbid TBI: high anticholinergic profiles can worsen cognition. Sertraline and prazosin are usually well-tolerated.
- MDMA-assisted psychotherapy: FDA declined approval in 2024. Not routinely available.

What tips the choice

Newly diagnosed PTSD with no strong comorbidity signal: sertraline or paroxetine (or venlafaxine XR off-label). Give it 8 to 12 weeks before judging response. Prominent nightmares and sleep disturbance: add prazosin. Consider trazodone or a DORA on top for sleep initiation. Refractory to SSRI or SNRI at adequate dose: switch class, or augment with risperidone or quetiapine. Comorbid depression: SSRI or SNRI covers both. Comorbid SUD: treat both, avoid benzodiazepines. Older adult: sertraline or escitalopram at lower dose. Veteran with combat-related PTSD: same algorithm, and VA-DoD guidelines specifically recommend trauma-focused therapy and against benzodiazepines and against atypical monotherapy.

Watchouts

- Benzodiazepines can interfere with extinction learning and worsen long-term outcomes in PTSD.
- Prazosin orthostasis: titrate slowly and warn the patient about lightheadedness after the first dose.
- Higher SSRI doses are often needed for PTSD than for depression. Adequate trial is at adequate dose for 8 to 12 weeks.
- Modest effect sizes are the norm: response rates around 60 percent for some symptom improvement, remission less common.
- Comorbid substance use is common. Screen and treat both.
- Combined medication plus trauma-focused therapy outperforms either alone for moderate to severe PTSD.

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