

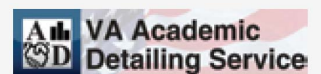
VA



U.S. Department
of Veterans Affairs

A VA Clinician's Guide to Managing Posttraumatic Stress Disorder

Improving Quality of Life Through the Use of
Evidence-Based Medicine



*Real Provider Resources
Real Patient Results*

A VA Clinician's Guide to Managing Posttraumatic Stress Disorder

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The Management of Posttraumatic Stress Disorder

Posttraumatic Stress Disorder (PTSD) is a complicated disorder with many co-occurring symptoms and sequelae. It is frequently seen in our Veteran population, and among new Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF) Veterans, PTSD is the most common mental health diagnosis.¹ Along with PTSD symptoms, it is common to see persistent difficulties with interpersonal relationships and mood, complaints of chronic pain, sleep disturbances, and somatization. It has also been found that Veterans with combat-related mild traumatic brain injury are more susceptible to developing PTSD.² Most importantly, people can recover from PTSD as there are several very effective evidence-based treatments that can be utilized.

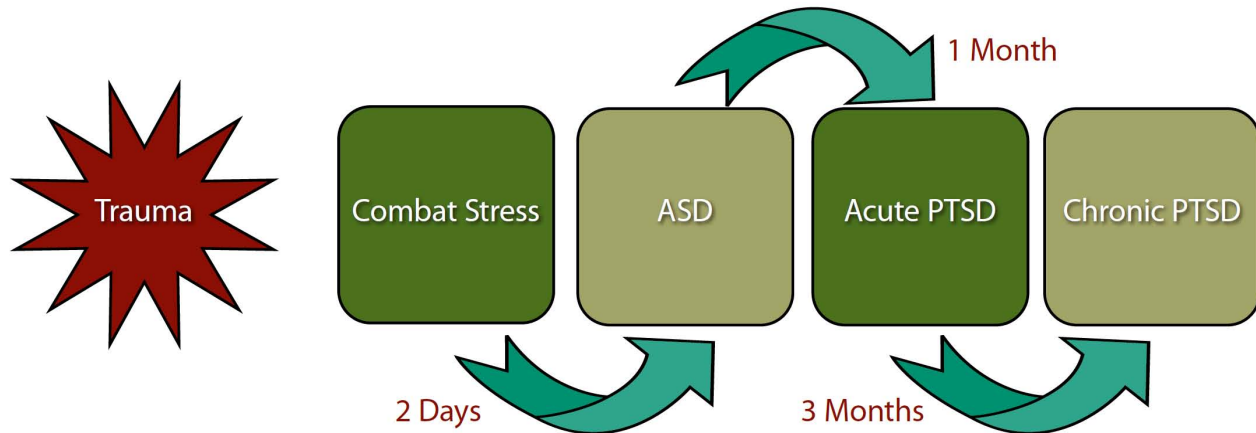
Our Veteran population and PTSD

- **PTSD is a growing diagnosis.** From 2004 to 2008, the number of individual Veterans seeking help for PTSD increased from 274,000 to 442,000.²
 - **Comorbid psychiatric disorders are prevalent in this patient population,** including substance abuse, depression, anxiety, and bipolar disorder.
 - Patients with PTSD are **six times more likely to attempt suicide** than the general population.³
-

There are many effective evidence-based treatments for PTSD, and new data suggests that changes to previously accepted therapies may be necessary in the management of our Veteran population.

Initial Treatment Selection

Initial treatment selection is based on the timeline of the stress reaction. The goal of early treatment is to reduce the development of acute and chronic PTSD.



ASD = Acute Stress Disorder, PTSD = Posttraumatic Stress Disorder

Assessing Response to Therapy

Good clinical care requires that clinicians monitor patient progress. It is increasingly recognized that incorporating a rating scale into clinical practice can assist the clinician in evaluating the patient's current status.

- ➔ The PTSD Checklist (PCL) is a 17-item, self-reported measure of the 17 DSM-IV symptoms of PTSD. The PCL has a variety of purposes, including:
 - ❖ Screening individuals for PTSD
 - ❖ Diagnosing PTSD
 - ❖ **Monitoring symptom change during and after treatment**
- ➔ The PCL takes 5–10 minutes to complete and patients can self-administer while in the waiting room.
- ➔ A 5 point change represents response to therapy.⁴
- ➔ A 10 point change represents a clinically significant change.⁴
- ➔ The PCL-5 is similar to the PCL but assesses the 20 DSM-5 symptoms of PTSD. It is expected that a clinically meaningful change in scores will be similar to the 17-item PCL.

The PCL should be used periodically to assess response to therapy and support clinical decision making.

Acute Stress Disorder Treatment

Acute interventions to prevent PTSD include:

- Education and normalization
- Brief psychotherapy sessions
 - ❖ Exposure
 - ❖ Cognitive restructuring
- Management of acute symptoms
 - ❖ Sleep/hyperarousal
 - ❖ Pain
- Social & spiritual support

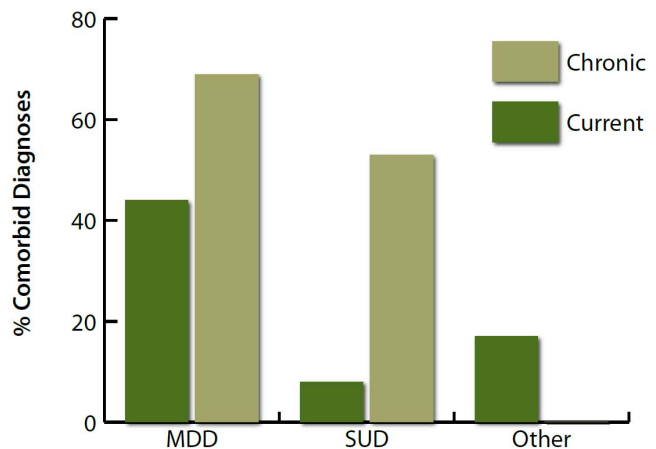
The use of benzodiazepines or other pharmacotherapies in this population is not recommended and has not been shown to prevent the development of PTSD.²

Posttraumatic Stress Disorder

Medical and mental health disorders, along with psychosocial problems, commonly coexist with PTSD.^{2,5}

There are many approaches to treating PTSD; therefore, treatment selection should be made on a case by case basis and take into consideration co-occurring symptoms and sequelae, effectiveness, tolerability, and cost.

Psychiatric Comorbidity with PTSD in Veterans since September 11, 2001⁵



Data from 365 US military Veterans. Disorder is considered current if criteria for the disorder have been met in the month prior to interview. Chronic is defined as both current diagnosis and meeting the diagnosis criteria in the past.

MDD = Major Depressive Disorder, SUD = Substance Use Disorder

VA/DoD 2010 Guidelines: Stepped Care Treatment of PTSD²



Non-Pharmacologic Therapies

Several clinical trials have demonstrated that cognitive therapies are an effective intervention in patients with PTSD and treatment gains may last up to two years.^{2,6-8} These therapies are trauma-focused psychotherapeutic interventions that include components of exposure and/or cognitive restructuring or stress inoculation training.⁶⁻⁸ The following is a partial list of current intervention-based conditioning approaches. While they have empirical validity, our most complicated Veterans often need a more comprehensive and synthetic approach, which should include evidence-based treatment whenever possible. If, however, it seems more appropriate to optimize function rather than reduce symptoms, supportive interventions may be found in outpatient clinics or Vet Centers.^{2,9} Veterans with a substance use disorder should also receive treatment concurrently with their PTSD treatment.

Veterans diagnosed with PTSD should be offered trauma-focused psychotherapeutic interventions.

Psychotherapy Interventions for Treatment of PTSD ²	
Psychotherapy Classification	Processes
Cognitive-based	Emphasize cognitive restructuring; relaxation techniques; discussion/narration of the traumatic event
Exposure-based	Psychoeducation; imaginal or narrative exposure; in-vivo exposure; processing of thoughts and emotion
Stress Inoculation	Coping/anxiety management skills (deep muscle relaxation, breathing control, assertiveness, thought stopping, positive thinking, self-talk); in-vivo exposure
Eye Movement Desensitization and Reprocessing (EMDR)	Access disturbing image with associated body sensation, relaxation/self-monitoring techniques, alternating eye movements

Pharmacotherapy

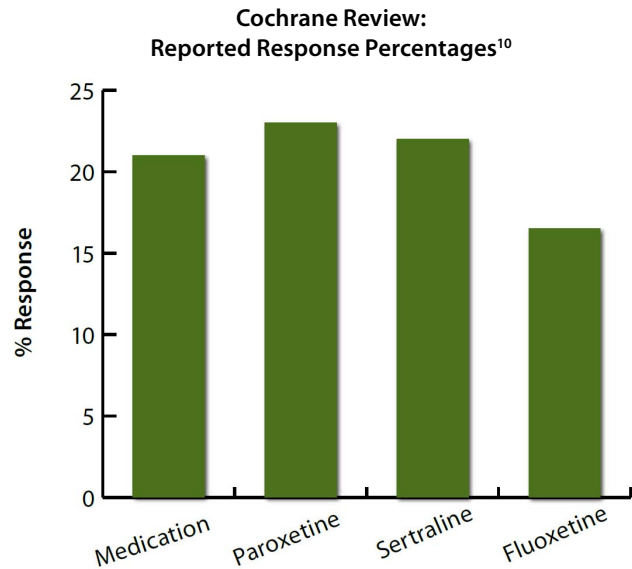
Pharmacotherapy should be considered as one aspect of a broader management plan for PTSD. SSRIs and the SNRI venlafaxine should be used as first-line psychotropics.

- The SSRIs paroxetine, sertraline, and fluoxetine have the largest collection of evidence showing their efficacy in this population.^{2,10}
- Evidence also supports the SNRI venlafaxine. Remission rates at 24 weeks were reported to be 51% versus 38% for placebo ($p = 0.01$, NNT = 8).¹¹
- Long-term efficacy is reported for SSRIs and venlafaxine.¹¹⁻¹³
- Studies indicate that while some patients respond early in treatment, some may require >3 months of pharmacotherapy, especially those with greater symptom severity.^{12,13}

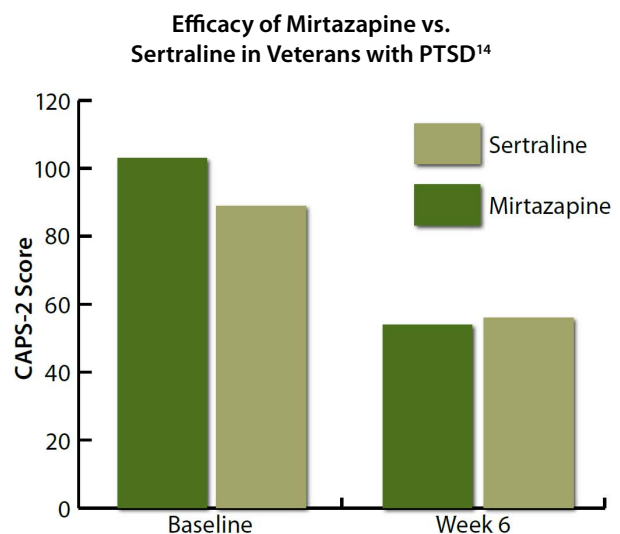
Monotherapy with an antidepressant should be optimized using the maximum tolerable dose for a minimum of 8 weeks before progressing to the next treatment strategy.

Other Antidepressants

Clinical trials have shown promising results for mirtazapine, amitriptyline, imipramine, phenelzine, and nefazodone for the treatment of PTSD but are limited by small sample sizes, open label design, or medication safety/side effect profiles.¹⁴⁻¹⁷ These antidepressants should be reserved for patients who have failed SSRI or SNRI monotherapy. Monitoring side effects is especially important during treatment with nefazodone or phenelzine.



Number needed to treat analysis revealed that treatment with medication resulted in a 21% response rate compared to placebo over an average of 11 weeks. Of the medication classes, evidence of the treatment efficacy was most convincing for the SSRIs. Individual medication response rates were calculated to be 23% for paroxetine, 22% for sertraline and 16.5% for fluoxetine. Clinician-Administered PTSD Scale score reduction: SSRI (WMD = -5.79, CI -8.9 to -3); paroxetine (WMD = -10.49, CI -13.87 to -7.11); sertraline (WMD = -3.78, CI -6.9 to -0.65). Significant treatment effects were not seen with citalopram and fluoxetine presumably because of small sample sizes. WMD = Weighted Mean Difference

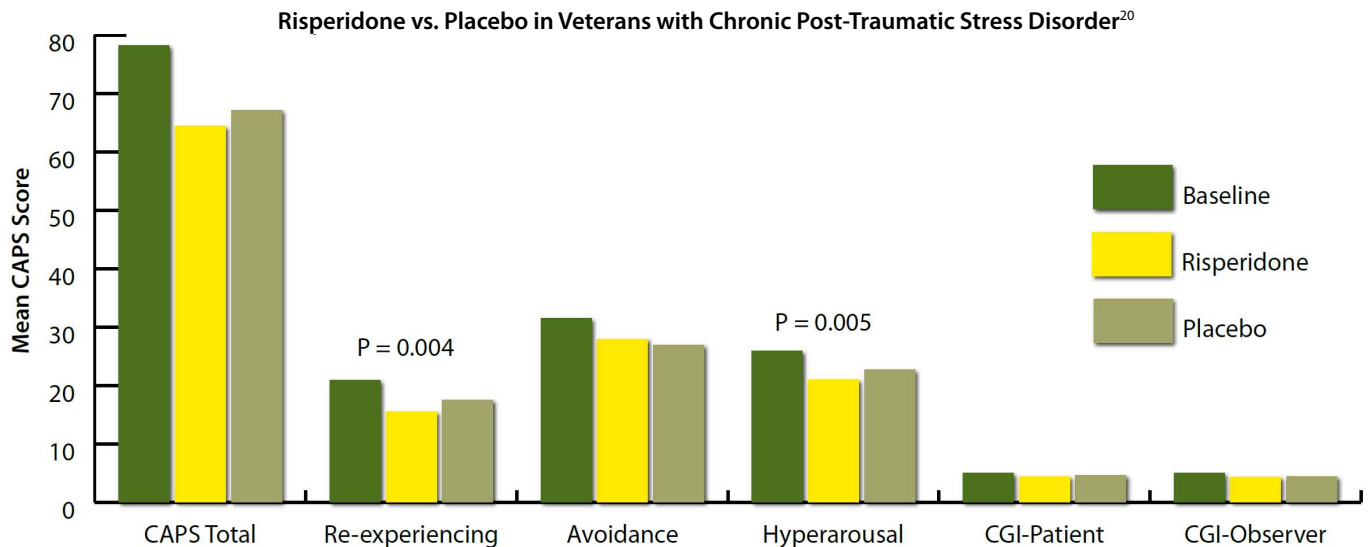


This open label study found mirtazapine to be as efficacious as sertraline in Korean Veterans ($n = 100$); CAPS-2 Score = Clinician-Administered PTSD Scale

Antipsychotic Medications

To date, two small placebo-controlled trials have assessed the use of atypical antipsychotics as monotherapy in the treatment of PTSD. Olanzapine was found to not have significant improvement over placebo, whereas risperidone showed modest improvement in global symptoms.^{18,19} The results for risperidone were in non-combat related PTSD, and newer data with adjunctive antidepressants indicate that risperidone is no better than placebo in our patient population.^{19,20}

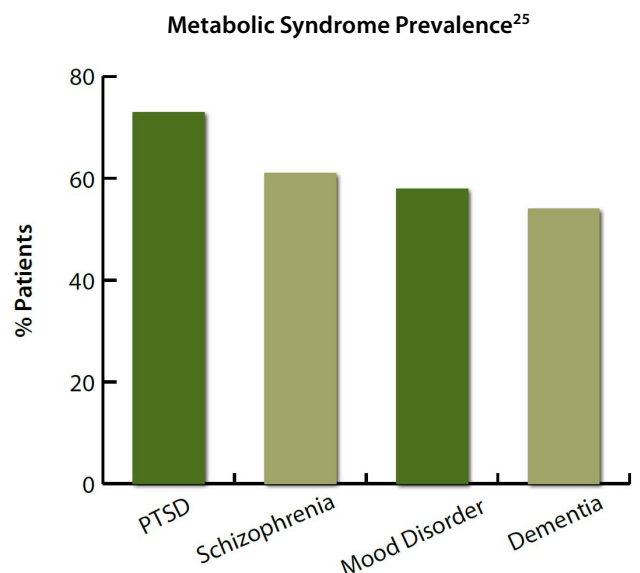
There is insufficient evidence to warrant the use of antipsychotic monotherapy for the treatment of PTSD.^{2,18,19}



No difference was found at 6 months between adjunctive risperidone (n = 133) and placebo (n = 134) for reducing CAPS total score in veterans with treatment resistant PTSD. In addition, risperidone did not reduce symptoms of depression, anxiety, or patient and observer rated CGI. In post hoc analysis there was statistical improvement in the re-experiencing and hyperarousal symptom clusters; however, these differences have a small effect size and questionable clinical significance. This study cannot rule out the possibility that risperidone treatment addresses a real clinical need for some patients. CGI = Clinical Global Improvement; CAPS = Clinician-Administered PTSD Scale

There is limited evidence for the use of atypical antipsychotics in PTSD treatment, and they can potentially cause significant harm; thus, their routine use cannot be recommended and discontinuation should be considered.^{2,20-24}

- ➔ Most antipsychotic clinical trials are small, have high placebo response rates, and have questionable clinical significance.
- ➔ Antipsychotics have little to no effect in global improvement.²⁰⁻²⁴
- ➔ Cardiometabolic risks of antipsychotics are at least equivalent to other disorders if not higher in patients with PTSD.^{25,26}

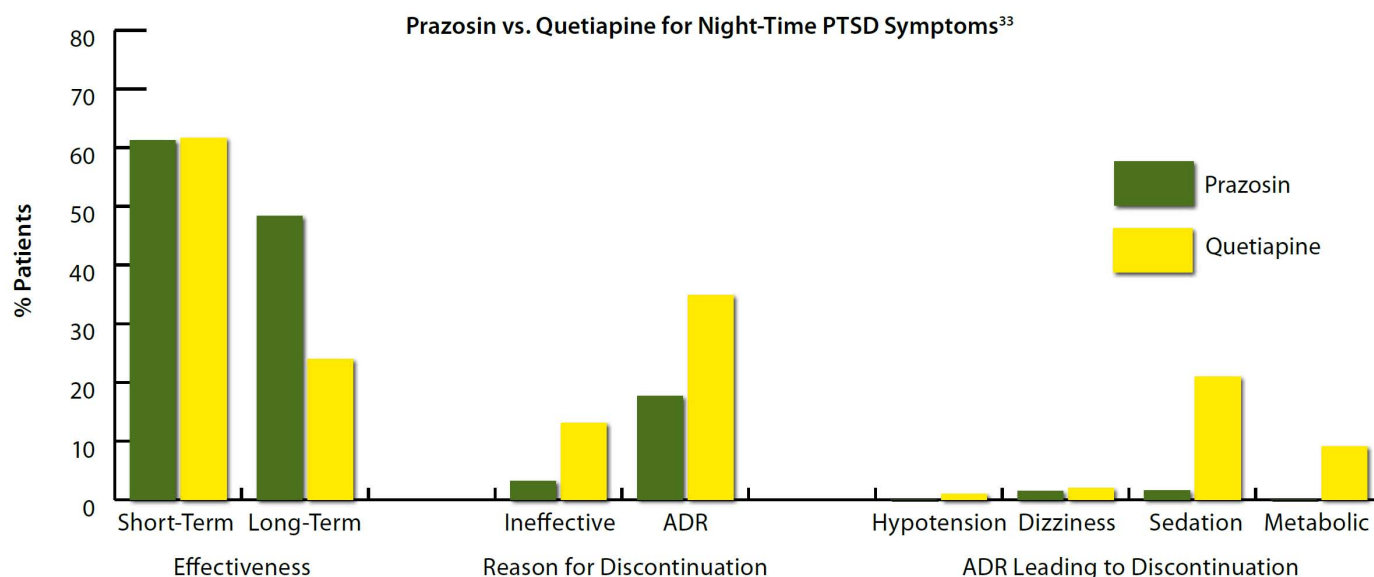


Results are adjusted for sex and age (n = 203). Type of antipsychotic did not vary between groups. Duration was shorter for dementia (44mo) vs. schizophrenia (253mo), PTSD (173mo), and mood disorder (129mo). The rates of metabolic syndrome were statistically equivalent to (and numerically worse than) those with schizophrenia (longer duration on antipsychotic).

Trauma Nightmares and Sleep Disturbances

Many Veterans with PTSD suffer from disrupted sleep patterns, including nightmares and frequent awakenings. These symptoms are often highly distressing to the Veteran, affecting approximately 70% of patients with PTSD.^{27,28}

- ➔ Sleep hygiene and cognitive behavioral therapy (CBT) can improve sleep quality by decreasing sleep onset and increasing sleep duration.^{2,29,30}
- ➔ Several small placebo-controlled trials have found that prazosin is significantly superior to placebo for reducing trauma nightmares and improving sleep quality.^{27,31-33}
- ➔ When properly titrated, prazosin is well tolerated and has not been shown to cause significant changes in blood pressure.^{27,31-33}



This retrospective chart review (n = 237) found that prazosin and quetiapine had similar short-term (<6mo) response rates. However, patients that were given prazosin were significantly more likely to continue their therapy (p < 0.001). More patients discontinued quetiapine therapy because of ineffectiveness (p = 0.003) and side effects, including sedation (p < 0.001) and metabolic changes (p = 0.014). ADR = Adverse Drug Reaction.

Prazosin is a reasonable option for adjunctive treatment of trauma nightmares and sleep disturbances in Veterans with PTSD. Studied prazosin doses range from 1–15mg with an average of 9–13mg nightly.^{27,31-33}

Suggested Prazosin Titration Schedule to Reduce Orthostatic Side Effects	
Days 1–3	1 mg
Days 4–7*	2 mg
Week 2	4 mg
Week 3	6 mg
Week 4	10 mg

*Increase dose if nightmares are still present and adverse effects are absent or mild. After week 4 the dose can be increased weekly by 5 mg increments until symptoms resolve or side effects prohibit an increase in dose. If therapy is interrupted for 3 or more days, reinitiate at lowest dose and re-titrate according to schedule.

Benzodiazepines in PTSD

- ➔ There is no evidence that benzodiazepines reduce the core symptoms of PTSD or work for PTSD-related sleep dysfunction.³⁴⁻³⁶
- ➔ Withdrawal of benzodiazepines is difficult in this population and can result in increased anxiety, sleep disturbances, rage, hyper-alertness, increased nightmares, and intrusive thoughts.³⁶
- ➔ Withdrawal effects have been documented with as little as 5 weeks of therapy.³⁶
- ➔ Risks outweigh the benefits for the chronic use of benzodiazepines in PTSD.

Benzodiazepine Equivalent Doses and Suggested Taper ^{37,38}						
	Chlordiazepoxide	Diazepam	Clonazepam	Lorazepam	Alprazolam	Temazepam
Approximate Dosage Equivalents	10 mg	5 mg	0.25–0.5 mg	1 mg	0.5 mg	10–20 mg
Elimination Half-Life	>100 hr	>100 hr	20–50 hr	10–20 hr	12–15 hr	10–20 hr
Benzodiazepine Taper						
<ul style="list-style-type: none"> • Switching to a longer acting benzodiazepine may be considered if clinically appropriate • High-dose alprazolam may not have complete cross-tolerance, a gradual switch to diazepam before taper may be appropriate • Reduce dose by 50% the first 2–4 weeks; then maintain on that dose for 1–2 months; then reduce dose by 25% every two weeks • Tapering at a faster rate may result in increased withdrawal symptoms and an unsuccessful taper • Other treatment modalities (e.g., antidepressants) for anxiety should be considered if clinically appropriate 						

The routine use of benzodiazepines is not recommended in patients with PTSD and discontinuation should be considered.

Adjunctive Treatment: Psychosocial Rehabilitation

- The longer or more severely symptomatic the patient, the more important it is to think through the entire spectrum of symptoms, interventions, and approaches.
- Chronic PTSD may result in a persistent incapacitating mental illness marked by severe and intolerable symptoms; marital, social, and vocational disability; and extensive use of psychiatric and community services.²

Treatment	Recommendation
Psychosocial Rehabilitation	<ul style="list-style-type: none"> • Family psychoeducation, supported employment, education, and/or housing may benefit Veterans with PTSD.² • If psychosocial problems are related to PTSD core symptoms, ensure that rehabilitation techniques are used as a contextual vehicle for alleviating PTSD symptoms. • Psychosocial problems should be addressed concurrently or shortly after treatment of PTSD.²

Therapeutic interventions that facilitate generalizing skills for coping with PTSD, such as case management and psychosocial rehabilitation should be offered when needed and sometimes benefit the Veteran with chronic PTSD more than psycho- or pharmaco- therapy.²

Adjunctive Treatment: Complementary and Alternative Medicine	
Treatment	Recommendation
Spiritual Support	<ul style="list-style-type: none"> • Loss of religious faith has been associated with greater utilization for mental health services among military Veterans in treatment for PTSD.^{2,33} • Assess for spiritual needs and facilitate access to spiritual/religious care when sought.²
Biomedical Somatic Therapies	<ul style="list-style-type: none"> • There is insufficient evidence to recommend the use of Biomedical Somatic Therapies as first line treatment in PTSD.² • Initial findings indicate that repetitive Transcranial Magnetic Stimulation and Electroconvulsive Therapy may provide possible benefits in chronic, treatment-resistant PTSD.³⁹⁻⁴² However, larger more robust trials are needed.
Acupuncture	<ul style="list-style-type: none"> • Though limited, studies show that acupuncture significantly improves PTSD core symptoms and associated symptomatology (chronic pain, depression, insomnia, anxiety, or substance abuse).^{2,43}
Other Complementary and Alternative Treatments	<ul style="list-style-type: none"> • Approaches such as mindfulness, yoga, massage, and others that promote relaxation have not been shown to be effective. • Other alternative therapies (natural products, exercise and movement, energy medicine, animal-assisted therapy) do not have supporting evidence for their use in PTSD but may facilitate patients' engagement in medical care.²

Though the evidence is sparse for the use of complementary and alternative treatments in PTSD, they may be considered as adjunctive approaches to address hyperarousal symptoms and comorbid conditions like pain.

Summary of Pharmacotherapy in PTSD²

		Global Improvement	Re-experiencing	Avoidance	Hyperarousal
SSRIs	Fluoxetine	X	X	X	X
	Sertraline	X	X	X	X
	Paroxetine	X	X	X	X
SNRIs	Venlafaxine	X	X	X	X
TCAs	Amitriptyline	X	X		X
	Imipramine	X	X		X
MAOIs	Phenelzine	X	X		X
Other Antidepressants	Mirtazapine	X	X		X
	Nefazodone	X	X		X
Sympatholytics*	Prazosin	X	X		X

*Agents to be used as adjunctive therapies; MAOI = Monoamine Oxidase Inhibitor; SSRI = Selective Serotonin Reuptake Inhibitor; SNRI = Serotonin Norepinephrine Reuptake Inhibitor; TCA = Tricyclic Antidepressant

These are general recommendations only; specific clinical decisions should be made by the treating provider based on an individual patient's clinical condition.

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These are general recommendations only; specific clinical decisions should be made by the treating provider based on an individual patient's clinical condition.

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