

# PTSD and Benzodiazepines: A Myth Agreed Upon

## ABSTRACT

Evidence-based clinical practice guidelines have become increasingly prominent as a way to increase stability and uniformity in treating particular conditions. This article compares and contrasts the clinical guidelines regarding prescription of benzodiazepines for patients with PTSD diagnoses from four national and international groups and their three updates. A brief history of the benzodiazepines is described, along with the focus on and persistence of misinterpretations of the potential adverse effects that can be compared with Napoleon's famous quotation, "History is a myth that men have agreed upon."

Benzodiazepines are not considered specific for the "core symptoms" of PTSD (intrusive thoughts/reexperiencing, emotional numbing, hyperarousal, avoidance) and they have a definite abuse and dependence potential. But PTSD is often accompanied by the symptoms of anxiety and insomnia, and in spite of the fact that benzodiazepines treat these symptoms possibly better than any other class of drugs, they are persistently viewed through a negative lens. Research findings of favorable effects of benzodiazepines in patients with PTSD are often given short shrift. For example, many of the evidentiary articles that are cited repeatedly in all of the published guidelines for using benzodiazepines are quite dated—some as old as two decades—and some include sample sizes as small as  $n=4$ , in one case.

This paper encourages physicians to avoid reflexively embracing the published guidelines, and give thoughtful consideration to this class of medication for appropriate patients with PTSD diagnoses when there is a clear indication for them.

## PTSD and Benzodiazepines: A Myth Agreed Upon

Napoleon Bonaparte was not only a warrior; he was also a shrewd propagandist. During his first campaign in Italy, he carefully crafted reports from the battlefield, designed to increase his glory while masking the ruthlessness with which he plundered the country ... “Even when I am gone, I shall remain in people's minds the star of their rights, my name will be the war cry of their efforts, the motto of their hopes.” [1] The French general summed it up with, “History is a myth that men have agreed upon.” This might be said of benzodiazepines as well.

Benzodiazepines are highly effective, safe and versatile medications that treat insomnia, muscle spasm, seizures, agitation, alcohol withdrawal, and in particular, anxiety. They are unrivaled in their overall effectiveness and safety for these conditions. Yet there has been an unremitting drumbeat of negativity about this class of medication that has succeeded in fostering its disapprobation or complete absence from the most highly respected clinical guidelines for posttraumatic stress disorder (PTSD), acute stress reaction (ASR), and acute stress disorder (ASD) [2-8]. This would seem to reflect the negative and avoidant manner in which benzodiazepines have historically been treated, and continue to be treated relative to PTSD. It is useful to review the history of this class of medication to understand where this negativity came from, and why it has flourished.

### A BRIEF HISTORY OF BENZODIAZEPINES

The first benzodiazepine, chlordiazepoxide (*Librium*), synthesized in 1955, showed strong sedative, anticonvulsant and muscle relaxant effects, and was marketed in 1960. Diazepam (*Valium*) was marketed in 1963. [9] Diazepam was the top-selling pharmaceutical in the United States from 1969 to 1982, with peak sales in 1978 of 2.3 billion tablets. [10] The risk of dependence became evident in the 1980s, and benzodiazepines were subsequently responsible for the largest-ever class-action lawsuit against drug manufacturers in the United Kingdom. The court case against the drug

manufacturers never reached a verdict; but led to changes in the British law, making class action law suits more difficult to effect

As a resident fellow in Forensic Psychiatry at the Federal Correctional Institution in Butner, North Carolina, in 1983, I discovered that benzodiazepines were almost entirely proscribed in penal systems nationwide. The relatively uncommon dependence and abuse issues were just beginning to come into focus at that time, and the concern was raised that we are creating a nation of addicts, rather than asking how or why the population became so anxiety-ridden. My research resulted in a publication of recommended guidelines for use in correctional facilities [11]. Little has changed since that time, as is apparent in evaluating the details of the research supporting recent national and international guidelines.

## THE GUIDELINES

In reviewing these guidelines and analyzing the references listed to support their recommendations, we find a repetition of many of the same studies cited. That is not necessarily a problem; but many of these papers are quite dated, and many draw their conclusions from very small sample sizes. Even in studies with larger sample sizes, positive results are often overlooked, ignored or reported in a dismissive manner. This paper reviews the conclusions and recommendations of these guidelines, followed by an examination of the articles cited to support the recommendations. (Reference numbers in brackets have been changed from their numbers in the original document to coincide with their number in the References list at the end of this paper).

### The APA Guidelines [2]

The 2004 APA guideline for PTSD and ASD has a relatively simple coding system [Table 1]. Benzodiazepines are classed as “III” which is defined as: “May be recommended on the basis of individual circumstances,” and are described as follows: “Benzodiazepines may be useful in reducing anxiety and improving sleep ... However, clinical observations include the possibility of dependence, increased

incidence of PTSD after early treatment with these medications, or worsening of PTSD symptoms after withdrawal of these medications.” Four references are cited to support the above statement [12-15]. In a later section, “Review and Synthesis of Available Evidence,” the document concludes that benzodiazepines “cannot be recommended as monotherapy for PTSD patients, despite their proven efficacy in generalized anxiety disorder,” and, “Despite widespread use in treatment of PTSD, their utility in PTSD has not been adequately evaluated.” Two additional references are cited [16,17].

#### The APA Guideline Watch [3]

The March, 2009 Update to the APA Guidelines for PTSD does not mention benzodiazepines.

#### The VA-DoD Guidelines [4]

In the 175-page Veterans Affairs/Dept. of Defense (VA-DoD) Guidelines for PTSD, a third derivative disorder is added: Acute Stress Reaction (ASR). The recommendations regarding benzodiazepines in this document are both copious and abstruse [Table 2]. The legends may serve an academic interest, but they offer little help to the clinician in the decision-making process. For example, for Acute Stress Reaction (ASR), benzodiazepines are placed in the “Some Benefit” box with the recommendation “Insufficient evidence to recommend for or against — the clinician will use clinical judgment,” (designated “R-I”). For Acute Stress Disorder (ASD), benzodiazepines are listed in the “Unknown” benefit box. While short-term use of benzodiazepines (less than 10 days) is recommended for acute symptom management in ASR and ASD, it is discouraged for longer use in those disorders. Finally, for Posttraumatic Stress Disorder (PTSD), the VA-DoD Guidelines are unequivocal, stating not only that there is “No Benefit” but also warning of potential “Harm” if they are used [Table 3] (p. I-5).

References cited to support the VA-DoD recommendations and non-recommendations are the same as in the APA Guidelines [13-15], along with one additional reference [18].

Consensus Statement on Posttraumatic Stress Disorder From the International Consensus Group on Depression and Anxiety [5]

Regarding benzodiazepines, this paper states the following:

“No studies support the efficacy of benzodiazepines in PTSD. On the contrary, some evidence suggests that the clinical condition of patients with PTSD deteriorates when they are treated with benzodiazepines, with impairment of learning in a clinical situation and disturbing withdrawal symptoms.”

There are 15 references listed at the end of this Consensus Statement, but none are designated in the body of the paper to support the above statement.

Consensus Statement Update on Posttraumatic Stress Disorder From the International Consensus Group on Depression and Anxiety [7]

The 2004 Update of the 2000 Consensus makes the following statement regarding benzodiazepines: “The benzodiazepines are not effective for PTSD [16].” For sleep difficulty, the group “cautioned against the use of traditional benzodiazepines because of associated withdrawal symptoms, lack of efficacy in the treatment of depression and PTSD, and interactions with alcohol.” No other reference is cited.

National Institute for Clinical Excellence (NICE) [8]

The National Institute for Clinical Excellence in London has also published a set of guidelines for PTSD treatment. Under the heading of “Pharmacological and physical interventions for PTSD,” this 176-page text does not include a section on benzodiazepines, anxiolytics, sedatives or hypnotics. Benzodiazepines are mentioned only indirectly, as part of a study of combat veterans who had risperidone added to their previously prescribed medications, some of which were benzodiazepines. Also, under the heading of “Current clinical practice,” it is noted that “41% were taking benzodiazepines and related drugs,” concluding that “the use of [benzodiazepines] is likely not to conform to international guidelines.” [19].

## EXAMINATION OF THE REFERENCES CITED IN THE GUIDELINES

The APA Guidelines [2] cites 6 references in support of their conclusions and recommendations [12-17]. These references were published between 1990 and 2002.

The first citation [12] evaluated 22 subjects (14 men, 8 women) suffering PTSD symptoms from accidents or assaults (non-combat related). The treatment group was given temazepam 30mg for 5 days, reduced by half for 2 days, then discontinued; the control group was given a placebo. As would be expected, there was significant improvement in sleep duration in the temazepam group during the treatment, but no difference in sleep duration a week after medication was discontinued; and no difference in core PTSD symptoms (intrusive thoughts/reexperiencing, emotional numbing, hyperarousal and avoidance) at the end of the 6-week study. The authors did find, however, a correlation between reduced awakenings and improvement in PTSD symptoms, and for that reason, suggested the “possibility of a role for other interventions for reducing sleep disruption,” dismissing further consideration of the benzodiazepine that produced the good results.

The second citation [13] evaluated 162 trauma victims, 13 of whom reported “excessive distress at the 1-week assessments (e.g. panic anxiety, agitation, or persistent insomnia),” and were prescribed benzodiazepines. The “control” group was made up of 13 others, matched by gender and IES (Impact of Event Scale: intrusion/avoidance) score, which was similar in both groups. Yet — and importantly — they were *not* matched in their STAI (anxiety) or BDI (depression) scores, which were significantly (10%) higher to begin with in the benzodiazepine group. Not surprisingly, given the higher severity of symptoms in the benzodiazepine group, the control group fared better at the end of study. The authors admit that the study was “obviously limited by the lack of random assignment to groups and the small sample size,” and moreover, “Given the current design, one cannot rule out the possibility that benzodiazepines *did have a beneficial effect* on those trauma survivors who were *clinically identified as highly distressed*. Accordingly, these subjects *could have been worse without treatment*,” [emphasis added].

The third citation [14] was published in 1990, and states, “Worsening of symptoms with benzodiazepine discontinuation has also been reported.” This citation refers to a study of over 500 patients with combat-induced PTSD. One hundred sixteen (23%) received alprazolam treatment of 2-9 mg/day for 1-5 years. Seventy-nine undertook a withdrawal regimen; 34 reported some mild clinical withdrawal symptoms; and eight had severe withdrawal reactions — anxiety, sleep disturbance, rage, hyperalertness, nightmares and intrusive thoughts. Six of the eight reported homicidal ideation. All had a prior history of alcohol abuse or substance abuse, and several had previously violent histories, even having taken part in torture and killings in combat situations. The paper concludes, “All eight patients demonstrated severe reactions associated with discontinuation of alprazolam after long-term use.” The authors admit the possibility that “the severe discomfort caused by alprazolam withdrawal worsened a preexisting condition.” They recommended considering chlordiazepoxide — also a benzodiazepine, but longer-acting — as a substitute for alprazolam, noting its less-severe withdrawal symptoms.

The fourth study [15] cited was published in 2000, and is larger than any of the others cited in support of the recommendations in these guidelines. Five hundred forty-one veterans with PTSD were examined at baseline, and 370 were available at one-year follow-up. Half were diagnosed with comorbid substance use disorders; yet the study concluded that treatment with benzodiazepines *was not associated with adverse effects on outcome*. This would seem to contradict even the generally unchallenged admonishment to avoid benzodiazepine use in patients with comorbid substance abuse diagnoses, as well as the “concerns about addictive potential” so often mentioned along with benzodiazepines. Specifically, it concludes:

- Benzodiazepine use had no significant impact on clinical outcome in either substance abusers or nonabusers.
- Substance abusers [treated with benzodiazepines] had significant reductions in both alcohol problems and violence.
- Violence showed no significant time interactions with benzodiazepine use.

Ultimately, in addition to bringing into sharp question the common practice of forswearing benzodiazepines in the substance-abusing population, the study concludes, “[T]he therapeutic role of chronic benzodiazepines in PTSD is not clear.”

The fifth study cited [16] under the “Review and Synthesis of Available Evidence” section, is distinguished as “the only pertinent randomized, controlled trial” of benzodiazepines with PTSD patients. Similar to [14], this article was published in 1990 and also studied only alprazolam. Moreover, it studied *only ten subjects*. The authors conscientiously concluded that their study was “necessarily limited by the small number of subjects and the relatively large number of dropouts,” as well as the fact that theirs was a “treatment-refractory group with a long duration of illness” unsuccessfully treated by a number of antidepressants previously. These drawbacks notwithstanding, the results showed a “significant advantage for alprazolam over placebo” in the HAM-A scale (for Anxiety). Moreover, four of the six best responders to alprazolam showed a greater-than-20% improvement on both the HAM-A *and* the PTSD Scale (Intrusion/Avoidance).

In the final study cited [17], the authors followed a total of four men (n=4) within 1-3 weeks of a traumatic experience, and hypothesized that “consolidating sleep would be beneficial during the acute aftermath of trauma.” In fact, that is exactly what happened. Temazepam was prescribed for a week, and the results revealed that in *all four cases*, “improved sleep continued 1 week after the 7-day course of temazepam had been discontinued, and PTSD symptom severity was reduced.” The guidelines conclude, “Although [the study] suggested improvement, positive long-term outcome data have not been reported, and a controlled study did not show advantage over placebo.”

The VA-DoD Guidelines [4] cites four references [13,14,15,17], all the same as in the 2004 APA Guidelines. But the additional reference cited [18], published in 1997, may be the most problematic. This was a study of 632 military members at Tripler Army Medical Center over a 6-year period, “the vast majority of whom suffered from combat-related PTSD.” The “Abstract” to the paper states, “Historically, many PTSD patients were treated with benzodiazepines, often in high

dosages. The risks attendant to benzodiazepine management of PTSD, coupled with poor clinical outcome, prompted the staff to explore treatment alternatives.” The foregoing statements, in the *abstract* of the paper, represent the only mention of benzodiazepines in the entire article. There are no data, there are no studies cited or described, there are no further references to support the statements in the abstract.

The Consensus Statement on Posttraumatic Stress Disorder From the International Consensus Group on Depression and Anxiety [5], as previously mentioned, lists 15 references in the Reference List at the end of the article, but none is annotated to support the entirely negative comments in the article. Interestingly, though, a textbook on guidelines for traumatic stress published at the same time as this Consensus Statement, and edited by one of the Consensus authors [6] is much more positive and even-handed in the two short paragraphs that mention benzodiazepines. Regarding open trials with alprazolam and clonazepam, it states, “patients reported reduced insomnia, anxiety, and irritability, but no improvement in reexperiencing, avoidant, or numbing symptoms.” The second paragraph refers to a study [17] that found “pharmacotherapy specifically targeting disrupted sleep was associated with marked reduction in PTSD symptoms.” A co-editor of the textbook, from the National Center for PTSD in Vermont, suggested in his own paper [20], “three possible clinical indications for clonazepam: (1) acute stress reactions; (2) episodically in chronic PTSD when extreme anxiety interferes with the patient’s participation in treatment; and (3) in carefully selected patients with comorbid alcohol or substance abuse.”

The Consensus Statement Update on Posttraumatic Stress Disorder From the International Consensus Group on Depression and Anxiety [7] cites only one reference in support of their proscription of benzodiazepines [16], as in other Guidelines already discussed.

The National Institute for Clinical Excellence (NICE) [8] does not cite any specific study to support its dismissive treatment of benzodiazepines; but they mention that the current

clinical practice of prescribing benzodiazepines does not conform to international guidelines. The fact that 41% of PTSD patients *were* prescribed with benzodiazepines suggests that physicians are most likely following their own experience and choosing not to withhold a generally very beneficial and helpful medication for their patients. Moreover, this practice suggests that physicians are either not reading or dismissing the guidelines that go against the grain of their experience and observations.

## RECENT LITERATURE

Recent literature carries on the tendency to eschew benzodiazepines in general and for PTSD in particular.

A 2009 comprehensive review [21] of meta-analyses and treatment guidelines relative to benzodiazepines for PTSD states, “[D]ifferent from data emerging from the treatment of a range of other anxiety disorders, data from trials of benzodiazepines in PTSD were not persuasive.” Yet the authors support this by falling back to the same reference cited many times that actually showed *positive* results for both anxiety and PTSD core symptoms in “four of the six best responders” out of the total ten subjects [16]. Beyond that one reference, this comprehensive review mentions nothing more regarding benzodiazepines.

The most recent article found at the time of this writing is an Expert Review of the pharmacotherapy for PTSD [22], and states, “[T]he use of these agents for the management of PTSD symptoms remains controversial.” Supporting this is a repetition of the same articles previously cited [2, 7, 8, 13, 14, 16]. Data from an article not previously discussed [23] studied six patients, ages 31-74, in whom “Clonazepam therapy resulted in improvements in the frequency of both sleep-onset problems and early-morning awakenings,” compared with placebo. Yet they conclude that clonazepam’s effect “upon sleep-related PTSD symptoms were unimpressive.” The review goes on to cite a newer reference regarding prescribing benzodiazepines to substance abusers: “Patients report that CNS depressants, such as alcohol, cannabis, opioids, and benzodiazepines acutely improve PTSD symptoms” [24]. Benzodiazepines are not given credit for being not only the safest, but the only legitimate anti-anxiety

medication in that group. The last reference [25] in the review is from a pharmacologic review on PTSD that states, “Despite the frequent use of benzodiazepines in PTSD, randomized placebo-controlled trials do not suggest a role for these medications,” again citing the same studies [13,14 and 16], some of which clearly *do* support a significant and beneficial role for benzodiazepines for PTSD [16], and especially “highly distressed” PTSD patients [13].

## DISCUSSION

Significant in all of the guideline documents [2-8] are the repeated references to the same studies of benzodiazepines with PTSD patients; or no references at all. The 2004 APA Guideline [2] cites references [12-17] yet reasonably concludes that benzodiazepines “May be recommended on the basis of individual circumstances.” The March, 2009 Guideline Watch [3] makes no mention of benzodiazepines, hypnotics, or sedatives, letting the open-ended recommendation of 2004 stand. The VA-DoD Guideline [4] cites references [13,14,15, and 17] and supplies the most copious and confusing recommendations [Tables 2 and 3]. Piling Pelion onto Ossa, the VA-DoD Guidelines add a third disorder, Acute Stress Reaction (ASR), and then give different recommendations for benzodiazepines in each of the three disorders. The 2000 International Consensus Group [5] cites no references for their comments regarding benzodiazepines, and their 2004 Update [7] cites the well-worn reference [16]. The National Institute for Clinical Excellence [8] does not mention benzodiazepines as a potentially therapeutic medication or adjunct; but this is the only set of guidelines that points out the fact that benzodiazepines *are* prescribed to a sizeable minority of PTSD patients [19]. More recently, a 2009 comprehensive review [21] once again reaches back to reference [16]; and another in 2009 [22] does the same [13,14, and 16].

The two most egregious distortions occur in citing references [14] and [18]. The former is repeatedly cited as support for the “worsening symptoms following benzodiazepine discontinuation,” yet the study addresses *only* alprazolam, and only eight combat veterans out of 116 who took alprazolam, and who also had histories of violence and substance abuse. Moreover, the fact that the authors recommended considering

chlordiazepoxide as a substitute benzodiazepine was disregarded. The reference to [18] cites the negative statements regarding benzodiazepines in the abstract, without noting that there is not a single word or item of data describing any study in the body of the paper.

There is a clear and present concern regarding the safety of benzodiazepines potential to cause dependence and addiction. A comprehensive review of the benzodiazepines, published in 2000, offered the following: “[Benzodiazepines] ... can be addicting. These agents are often taken in combination with other drugs of abuse by patients with addiction disorders.” The authors recommend “caution ... when prescribing benzodiazepines to patients with a current or remote history of substance abuse.” They go on to point to a 1990 report by the American Psychiatric Association (APA) on benzodiazepine dependence, toxicity and abuse that indicated “11 to 15 percent of the adult population had taken a benzodiazepine one or more times during the preceding year, but only 1 to 2 percent have taken benzodiazepines daily for 12 months or longer.” [26]. This paper, though more comprehensive and recent and than many of the references cited, was not referred to in any of the agencies’ guidelines.

## SUMMARY

In the APA Guidelines, physician experience, preference in treatment and clinical judgment prevail. The gingerly manner in which benzodiazepines are recommended in other guidelines tends to disregard the substantial clinical experience that practicing psychiatrists and other physicians have had for many decades with these medications. Benzodiazepines do not provide a remedy for the core symptoms of PTSD – nightmares, intrusive thoughts, flashbacks or avoidance – and these medications should not be considered as a first-line treatment. They rarely turn out to be the most effective monotherapy for PTSD patients. In some cases, however, by alleviating the sleep disturbances and anxiety that accompany PTSD, benzodiazepines can facilitate a mitigation of the core symptoms, which may obviate the need for patients to turn to alcohol and/or illegal drugs. In that respect, benzodiazepines can be therapeutic for appropriately identified patients with PTSD.

A negative stamp can deter physicians from using benzodiazepines altogether for emotionally traumatized patients, fearing a lack of defense in the event of a poor outcome. Even more problematic, this negativity fosters a tendency to withdraw benzodiazepines from any PTSD patient, no matter how long or how well-stabilized they have been on the medication. As noted in the Risse article [14] cited in many of the guidelines, *withdrawing* a benzodiazepine, even on an appropriately cautious schedule, can initiate (or cause a relapse of) severe emotional problems. Several of the available guidelines can cause physicians to ask what kind of defense they would have in the event of a lawsuit by a patient with PTSD who has a bad outcome – of *any* kind – after prescribing or renewing benzodiazepines. The guidelines, with the exception of the APA Guidelines, provide little in the way of support. When there is a healthy minority of physicians who practice differently than the recommendations suggest, it may be reasonable to give more recognition to those standards of practice.

Future studies should move in two directions: First, being more specific in categorizing the diversity of the type of trauma. Combat trauma *vs.* motor vehicle accidents *vs.* sexual assault *vs.* natural disaster trauma – even flood disaster *vs.* fire – should be identified and perhaps tested separately, as well as differences in age and gender. Secondly, much larger populations of trauma victims need to be accessed. There are tens of thousands of such victims in all of the above categories across the country, and it would seem feasible to access larger subject groups in order to establish more specific guidelines.

Benzodiazepines are among the most widely prescribed medications [27]. For that reason, it behooves the committees responsible for writing guidelines not only to widen the research base on which their recommendations stand, but perhaps give more weight to the experience of the significant minority of clinicians who continue to prescribe this medication. It is important to recognize benzodiazepines' place in treating – not the diagnosis of PTSD alone, as it is fairly clear that they do not prevent the onset or continuation of the core symptoms – but the anxiety and insomnia that so commonly accompany PTSD.

TABLE 1

Each recommendation is identified as falling into one of three categories of endorsement, indicated by a bracketed Roman numeral following the statement. The three categories represent varying levels of clinical confidence regarding the recommendation:

- [I] Recommended with substantial clinical confidence.
- [II] Recommended with moderate clinical confidence.
- [III] May be recommended on the basis of individual circumstances.

TABLE 2 (Reprinted from [3], pp. AA3-4):

**Quality of Evidence (QE)**

- I** At least one properly done randomized controlled trial (RCT)
- II-1** Well designed controlled trial without randomization
- II-2** Well designed cohort or case-control analytic study
- II-3** Multiple time series, dramatic results of uncontrolled experiment
- III** Opinion of respected authorities, case reports, and expert committees

**Overall Quality**

- Good:** High grade evidence (I or II-1) directly linked to health outcome
- Fair:** High grade evidence (I or II-1) linked to intermediate outcome or moderate grade evidence (II-2 or II-3) directly linked to health outcome
- Poor:** Level III evidence or no linkage of evidence to health outcome

**Net Effect of the Intervention**

- Substantial:** More than a small relative impact on a frequent condition with a substantial burden of suffering; *or* a large impact on an infrequent condition with a significant impact on the individual patient level
- Moderate:** A small relative impact on a frequent condition with a substantial burden of suffering; *or* a moderate impact on an infrequent condition with a significant impact on the individual patient level
- Small:** A negligible relative impact on a frequent condition with a substantial burden of suffering; *or* a small impact on an infrequent condition with a significant impact on the individual patient level
- Zero or Negative:** Negative impact on patients; *or* no relative impact on either a frequent condition with a substantial burden of suffering; *or* An infrequent condition with a significant impact on the individual patient level

**RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS**

- A** A strong recommendation that the intervention is always indicated and acceptable
- B** A recommendation that the intervention may be useful/effective
- C** A recommendation that the intervention may be considered
- D** A recommendation that a procedure may be considered not useful/effective, or may be harmful
- I** Insufficient evidence to recommend for or against – the clinician will use clinical judgment.

TABLE 3 (Reprinted from [3], pp. I-5, I-6):

**B. Post-Traumatic Stress Disorder (PTSD) Pharmacotherapy  
Summary Table for PTSD Pharmacotherapy\***

<b>R*</b>	<b>Significant Benefit</b>	<b>Some Benefit</b>	<b>Unknown</b>	<b>No Benefit/Harm</b>
<b>A</b>	SSRIs			
<b>B</b>		TCAs MAOIs		
<b>C</b>		Sympatholytics Novel Antidepressants		
<b>I</b>			Anticonvulsants Atypical Antipsychotics Buspirone Nonbenzodiazepine hypnotics	
<b>D</b>				Benzodiazepines Typical Antipsychotics

**RECOMMENDATIONS**

**MONOTHERAPY:**

1. Strongly recommend selective serotonin reuptake inhibitors (SSRIs) for the treatment of PTSD.
2. Recommend tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs) as second-line treatments for PTSD.
3. Consider an antidepressant therapeutic trial of at least 12 weeks before changing therapeutic regimen.
4. Consider a second-generation (e.g., nefazodone, trazodone, venlafaxine, mirtazapine, bupropion, etc) in the management of PTSD.

**AUGMENTED THERAPY FOR TARGETED SYMPTOMS:**

5. Consider prazosin to augment the management of nightmares and other symptoms of PTSD.
6. Recommend medication compliance assessment at each visit.
7. Since PTSD is a chronic disorder responders to pharmacotherapy may need to continue medication indefinitely; however it is recommended that maintenance treatment should be periodically reassessed.
8. There is insufficient evidence to recommend a mood stabilizer (e.g. lamotrigine) for the treatment of PTSD.
9. There is insufficient evidence to recommend atypical antipsychotics for the treatment of PTSD.
10. There is insufficient evidence to support the recommendation for a pharmacological agent to prevent the development of PTSD.
11. Recommend against the long-term use of benzodiazepines to manage core symptoms in PTSD.
12. Recommend against typical antipsychotics in the management of PTSD.

## REFERENCES:

1. PBS. Napoleon, the Man and the Myth.  
[http://www.pbs.org/empires/napoleon/n\\_myth/self/page\\_1.html](http://www.pbs.org/empires/napoleon/n_myth/self/page_1.html). Accessed 3/12/10.
2. Ursano RJ, Bell C, Eth S, Friedman M, Norwood A, Pfefferbaum B, Pynoos RS, Zatzick DF, Benedek DM. Practice Guideline for the Treatment of Patients With Acute Stress Disorder and Posttraumatic Stress Disorder. American Psychiatric Association. November 2004, pp. 11, 13.
3. Benedek DM, Friedman MJ, Zatzick D, Ursano RJ. Guideline Watch (March 2009): Practice Guideline for the Treatment of Patients With Acute Stress Disorder and Posttraumatic Stress Disorder. Copyright © 2009. American Psychiatric Association.
4. Veterans Health Administration, Department of Defense. VA/DoD clinical practice guideline for the management of post-traumatic stress. Version 1.0. Washington (DC): Veterans Health Administration, Department of Defense; 2004 Jan.
5. Ballenger JC, Davidson JRT, Lecrubier Y, Nutt DJ, Foa EB, Kessler RC, McFarlane AC, Shalev AY. Consensus Statement on PTSD From the International Consensus Group on Depression and Anxiety. *J Clin Psychiatry* 2000;61 (suppl 5) pp.60-66.
6. Practice Guidelines from the International Society for Traumatic Stress Studies. Edited by Foa EB, Keane TM, Friedman MJ. Guilford Press, copyright 2000. pp. 95-96.
7. Ballenger JC, Davidson JRT, Lecrubier Y, Nutt DJ, Marshall RD, Nemeroff CB, Shalev AY, Yehuda R. Consensus Statement Update on Posttraumatic Stress Disorder From the International Consensus Group on Depression and Anxiety. *J Clin Psychiatry* 2004;65 (suppl 1) pp. 55-62.

8. Post-traumatic stress disorder: the management of PTSD in adults and children in primary and secondary care. National Guideline Clearinghouse. National Clinical Practice Guideline Number 26. Commissioned by the National Collaborating Centre for Mental Health. National Institute for Clinical Excellence (NICE). © The Royal College of Psychiatrists & The British Psychological Society. London, UK (2005).
9. Shorter E. Benzodiazepines. *A Historical Dictionary of Psychiatry*. Oxford University Press. 2005; pp. 41–42.
10. Sharon L (now Roth L). Benzodiazepines: Guidelines for use in correctional facilities. *Psychosomatics* 1984; Vol. 25, No. 10:784-788.
11. Sample I. Leo Sternbach's Obituary. *The Guardian* (Guardian Unlimited) Oct. 3, 2005. <http://www.guardian.co.uk/society/2005/oct/03/health.guardianobituaries>. Accessed 3-16-2010.
12. Mellman TA, Bustamante V, David D, Fins AI. Hypnotic medication in the aftermath of trauma. *J Clin Psychiatry* 2002; 63:1183-1184.
13. Gelpin E, Bonne O, Peri T, Brandes D, Shalev AY. Treatment of recent trauma survivors with benzodiazepines: a prospective study. *J Clin Psychiatry* 1996; 57:390-394.
14. Risse SC, Whitters A, Burke J, Chen S, Scurfield RM, Raskind MA: Severe withdrawal symptoms after discontinuation of alprazolam in eight patients with combat-induced posttraumatic stress disorder. *J Clin Psychiatry* 1990; 51:206–209.
15. Kosten TR, Fontana A, Sernyak MJ, Rosenheck R: Benzodiazepine use in posttraumatic stress disorder among veterans with substance abuse. *J Nerv Ment Dis* 2000; 188:454–459.

16. Braun P, Greenberg D, Dasberg H, Lerer B. Core Symptoms of Posttraumatic Stress Disorder Unimproved by Alprazolam Treatment. *J Clin Psychiatry* 1990;51:236-238.
17. Mellman TA, Byers PM, Augenstein JS. Pilot Evaluation of Hypnotic Medication During Acute Traumatic Stress Response. *J Traumatic Stress*, Vol. 11, No. 3, 1998.
18. Viola J, Ditzler T, Batzer W, Harazin J, et al. Pharmacological management of post-traumatic stress disorder: clinical summary of a five-year retrospective study, 1990-1995. *Military Medicine*. 162, 9:616. 1997.
19. Mellman TA, Clark RE, Peacock WJ. Prescribing patterns for patients with posttraumatic stress disorder. *Psychiatric Services*, December 2003. 54, 1618–1621.
20. Friedman MJ. Drug Treatment for PTSD. Reprinted from *Psychobiology of Posttraumatic Stress Disorder*. *Annals of the New York Academy of Sciences*. Vol. 821; June 21, 1997. pp. 359-371.
21. Stein DJ, Ipser J, McAnda N. Pharmacotherapy of posttraumatic stress disorder: a review of meta-analyses and treatment guidelines. Jan 2009. *CNS Spectr* 14:1 (Suppl 1) pp.25-31.
22. Alderman CP, McCarthy LC, Marwood, AC. Pharmacotherapy for post-traumatic stress disorder. *Expert Rev Clin Pharmacol*. 2009;2(1):77-86.
23. Cates ME, Bishop MH, Davis LL, Lowe JS, Woolley TW. Clonazepam for treatment of sleep disturbances associated with combat-related posttraumatic stress disorder. *The Annals of Pharmacotherapy*. Sept. 2004, Vol. 38. pp. 1395-1399.
24. Jacobsen LK, Southwick SM, Kosten TR. Substance use disorders in patients with post-traumatic stress disorder: a review of the literature. *Am J Psychiatry* 158,1184-1190 (2001).

25. Ahearn EP, Krohn A, Connor KM, Davidson JRT. Pharmacologic Treatment of Posttraumatic Stress Disorder: A Focus on Antipsychotic Use. *Annals of Clinical Psychiatry*, September/December 2003. Vol. 15, Nos. 3/4. pp 193-201.
26. Longo LP, Johnson B. Addiction: Part I. Benzodiazepines--Side Effects, Abuse Risk and Alternatives. *Am Fam Physician* 2000; 61:2121-8
27. U. S. Drug Enforcement Administration. Benzodiazepines.  
<http://www.justice.gov/dea/concern/benzodiazepines.html>. Accessed 3/26/10.