Benzodiazepines and the Treatment of Anxiety Disorders

Treatment Guidelines

All treatment guidelines recommend SSRIs as first line pharmacologic treatment for anxiety disorders.

Some treatment guidelines also include SNRIs as first-line treatment.

TCAs, with consideration of side effects, particularly overdose potential and sedation, are often recommended as 2nd line treatment.

Research evidence *does not* support the use of bupropion for the treatment of anxiety.

Guidelines	Panic	GAD
APA (2009)	Benzos - short term use No mono-therapy Scheduled dosing is preferred to prn dosing.	No guidelines
National Institute for Health and Care Exellence (NICE) (2011)	"Benzodiazepines, sedating antihistamines or antipsychotics should not be prescribed for the treatment of panic disorder"	"Do not offer a benzodiazepine for the treatment of GAD in primary or secondary care except as a short-term measure during crises."

	Benzodiazepines in the Treatment of PTSD
APA	While benzodiazepines can reduce anxiety and improve sleep, their efficacy in preventing PTSDor treating the core symptoms of PTSD has been neither established nor adequately evaluated. Concerns about addictive potential in individuals with comorbid substance use dis-orders may prompt additional caution regarding the use of benzodiazepines. Worsening of symptoms with benzodiazepine discontinuation has also been reported (158).
VA/DoD	-Uses graded system. A=evidence. B=weak evidence. I=inconclusive evidence. D=Potential for harm Benzodiazepines= D (HARM)
NICE	First line treatment -trauma-focused psychological therapy. Where sleep is a major problem for an adult PTSD sufferer, hypnotic medication may be appropriate for short-term use
ISTSS	No. "Currently no data support the efficacy of benzodiazepines for the treatment of "core" PTSD symptoms, such as re-experiencing, avoidance, negative alterations in cognition and mood and hyperarousal." Comorbid TBI - particular caution should be observed about the use of sedative medications

Psychopharmacology for Comorbid Anxiety and Alcoholism

-Use of benzos is controversial
-Most treatment guidelines recommend avoiding benzodiazepines in patients with alcohol dependence (other than time-limited use for ETOH withdrawal)
-Continuous use should be done cautiously
-Very little research data on other options

Benzodiazepines in the Elderly

-Metabolize less efficiently - drug effects last longer and drug accumulation occurs with regular use.

-Oversedation persists longer, is more marked in the elderly and may contribute to falls and fractures.

-Acute confusional states have occurred in the elderly even after small doses of benzodiazepines.

-can cause confusion, night wandering, amnesia, ataxia (loss of balance), hangover effects and "pseudodementia" (sometimes wrongly attributed to Alzheimer's disease) in the elderly and should be avoided wherever possible. Increased sensitivity to benzodiazepines in older people is partly because they metabolise drugs less efficiently than younger people, so that drug effects last longer and drug accumulation readily occurs with regular use. However, even at the same blood concentration, the depressant effects of benzodiazepines are greater in the elderly, possibly because they have fewer brain cells and less reserve brain capacity than younger people.

For these reasons, it is generally advised that, if benzodiazepines are used in the elderly, dosage should be half that recommended for adults, and use (as for adults) should be short-term (2 weeks) only. In addition, benzodiazepines without active metabolites (e.g. oxazepam [Serax], temazepam [Restoril]) are tolerated better

*from The Ashton Manual, retrieved online 11/15/2015

Benzodiazepines in Grief and Acute Stress

-Benzodiazepines are believed to interfere with memory consolidation, disrupting therapeutic memory processing. Could contribute to later development of PTSD or unresolved grief.

-May afford relief from the distress of catastrophic disasters, but if used for more than a few days they may prevent the normal psychological adjustment to such trauma. (Ashton Manual)

When prescribing Benzodiazepines

- Does it improve the patient's functioning?

If nothing changes, get rid of them.

- Recommend short-term use
- Preference for long-acting benzos (Clonazepam or Diazepam)*
- Tapering begins with the initial prescription
- Always emphasize the importance of therapy and/or need for skill development

*dementia study suggests short-acting for long-term use

Tapering Benzos

Many ways to taper – all recommend transitioning to either clonazepam or diazepam, then slowly tapering at 25% or less per week.

1. Decrease ≤ 25% per week OR
2. Reduce first 50% of the dose over 4-8weeks, then taper the final 50% more gradually as tolerated by the patient.

Dose equivalency charts vary:

Alprazolam 0.5mg = lorazepam 1 mg = diazepam 5mg =clonazepam 0.25mg (*Clinical Handbook of Psychotropic Drugs*)

Slow withdrawal schedules can be found in the Ashton Manual:
http://www.benzo.org.uk/manual/

Other medications while tapering
-Addition of anticonvulsants: tegretal, valproic acid and gabapentin may be useful for withdrawal. (*Handbook of Psychiatric Drug Therapy*)

From The Carlat Psychiatry Report Sept 2015, "What Psychiatrists Should Know about Sleep Medicine":

> **TCPR: How are you getting patients off benzos?**
>
> **Dr Rosenberg:** Based on some recent studies, I am using pregabalin (Lyrica) and finding that it is an excellent way to wean people off of benzodiazepines. We normally start them on Lyrica anywhere from 50–75 mg and begin to taper the benzo by about 50% every week or two. If they have problems tolerating the taper, we'll double the Lyrica to 150. Once the patient is off the benzos, we'll try tapering off the Lyrica over a week or so, but some patients want to stay on it, which is probably fine, because it's safe (Bobes J et al, Eur Psychiatry 2012;27(4):301–307).

Robert, Rosenberg, DO, FCCP, Medical director of the Sleep Disorders Center of Prescott Valley, AZ, and author of Sleep Soundly Every Night, Feel Fantastic Every Day *(Demos Medical Publishing, 2014*

Off-Label Medications for the Treatment of Anxiety Disorders*

Lyrica (pregablin)- GABA reuptake inhibitor

- Approved for GAD in Europe

-3 Drug-sponsored studies –more effective than placebo and equal to Xanax and Ativan

-Start 100mg qhs and gradually titrate to 300mg BID

-Side effects – dizziness, sedation, weight gain (5lb), addictive?

- no drug-drug interactions

Neuronin (gabapentin) – Modulator of GABA

-1 small placebo-controlled trial: > placebo for social phobia but overall response rates were low

-large double-blind study – rapid 4-day taper of Neurontin (1200mg to 800mg/day) was more effective than lorazepam taper in preventing relapse in alcohol withdrawal.

-Side effects: dizziness and sedation

Gabatril (tiagabine) –GABA A reuptake inhibition

-3 placebo controlled trial for GAD, no difference between gabatril and placebo but, among patients who tolerated it, some improvement

-Side effects: dizziness, headache, nausea, fatigue and somnolence

Topamax (topiramte) – Mechanism unknown

-Open trials in non-combat PTSD showed rapid improvement of some PTSD Symptoms at 50-100mg/day

-Placebo-controlled trials found ineffective, may have been due to large drop-out rates

Side effects: Cognitive Dulling and sedation

Seroquel XR (quetiapine XR) – atypical antipsychotic

-3 8wk placebo controlled studies for GAD, doses of 50-150mg were more effective than placebo in 2 of 3 studies. 300mg dose was either ineffective or provided no additional benefit.

-FDA rejected because long-term side effects

-Side effects: somnolence/sedation, weight gain

Hydroxyzine (Atarax, Vistaril) – antihistamine

-Not really off label, good efficacy data

-GAD –large randomized placebo-controlled trial found 50mg/day as effect as bromazepam 6mg/day (equivalent to diazepam 10mg/day)

*From: Carlat, D. (2009). Treatment for Anxiety Disorders. *The Carlat Psychiatry Report*, 7(11)