



GUIDELINES FOR THE USE OF BENZODIAZEPINES IN OFFICE PRACTICE IN THE STATE OF MAINE

Introduction: This is an evidence-based guideline for the use of benzodiazepines and related drugs in clinical office practice. Attached is a bibliography including earlier guidelines on which this guideline is partially based and websites, reviews, and clinical studies that provide supporting evidence. This guideline applies to benzodiazepines used primarily as anxiolytics and sedative/hypnotics, and to the related Z drugs, such as zolpidem, which, while structurally different from the benzodiazepines, produce similar pharmacologic effects and have similar abuse and dependence potential.

1. The patient and his caregivers will agree on one provider who will be the designated BZD prescriber for that patient. This designated prescriber will also be responsible for prescribing all other drugs with abuse potential that the patient will be maintained on for a period of time, specifically central nervous system stimulants and narcotics. The use of BZDs with long-term narcotics or stimulants is discouraged.

2. The principal indication for BZDs is for short-term treatment (2 to 6 weeks) of anxiety disorders. These conditions include generalized anxiety disorder, phobias, PTSD, panic disorder, and severe anxiety associated with depression, while waiting for the full effect of the antidepressant. While BZDs have been studied and utilized to treat these conditions they are not part of recommended first-line therapy for any of them. However, it is acceptable to use BZDs as adjuncts during initial treatment while waiting for definitive therapy with long-term medications and counseling to take hold. Continuing BZDs beyond 4 to 6 weeks will often result in loss of effectiveness, the development of tolerance, dependence and potential for withdrawal syndromes, persistent adverse side effects, and interference with the effectiveness of definitive medication and counseling. BZDs taken for more than 2 weeks continuously should be tapered rather than discontinued abruptly.

35 3. If in the judgement of the clinician, the patient will have difficulty
36 stopping the BZDs after the 2 to 6 week acute treatment period, then BZDs
37 should not be prescribed.

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40 4. Other indications for BZDs in the office setting:

41 Short-term treatment of insomnia (1 to 2 weeks)

42 As a muscle relaxant (1 to 2 weeks)

43 For urgent treatment of acute psychosis with agitation

44 As part of a protocol for treating alcohol withdrawal

45 As an adjunct for withdrawal from other addictions (less accepted)

46 Single-dose treatment of phobias, such as flying phobia

47 Seizures and certain other neurological disorders which will not be
48 addressed here

49 Sedation for office procedures

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51 5. BZDs may be used for longer than 6 weeks in the terminally ill, in the
52 severely handicapped patient, in certain neurological disorders, and as an
53 alternative to antipsychotics in the severely demented patient.

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55 6. There is evidence for the effectiveness of BZDs and other hypnotics in the
56 relief of short-term, but not long-term, insomnia. The treatment period
57 should not exceed 2 weeks. The only significant clinical difference between
58 older BZD hypnotics and the newer ones—zolpidem (Ambien), zaleplon
59 (Sonata), and eszopiclone (Lunesta) -- is the shorter half-life of zolpidem
60 and zaleplon (2 hours). All three have similar risks of dependence and
61 tolerance. A search for an etiology of the insomnia will be undertaken.
62 Sleep hygiene measures will be discussed.

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64 7. BZDs or other muscle relaxants are indicated for the short-term relief of
65 muscular discomfort associated with acute injuries and flare-ups of chronic
66 back pain. BZDs may be combined with analgesics and non-drug therapies
67 but not with other sedatives, hypnotics, or other muscle relaxants.

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69 8. Risks and side effects of BZDs will be reviewed, including the risk of
70 dependence. In the patient over 65, these will include the risk of falls,
71 cognitive impairment, and interactions with other medications and medical
72 conditions. Therefore BZDs should be used with caution in this age group.

73 Because of delayed metabolism and increased risk of side effects, the
74 starting dose should be one-half of the usual adult starting dose. The half-
75 life is prolonged significantly in the elderly.

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78 9. Contra-indications to BZDs are:

- 79 a) Pregnancy and the patient at risk for pregnancy. BZDs are category
80 D. For a hypnotic, zolpidem (Ambien), which is category B, should
81 be used. Patients who conceive while on BZDs should be tapered
82 completely off or to the lowest dose possible.
- 83 b) Active substance abuse, including alcohol.
- 84 c) Problems that would be aggravated by BZDs. These include
85 fibromyalgia, chronic fatigue syndrome, sleep apnea, impulse-
86 control problems, depression (except for short-term use to treat
87 associated anxiety), and kleptomania. They may worsen hypoxia
88 and hypoventilation in asthma, COPD, CHF, and other
89 cardiopulmonary diseases.
- 90 d) BZDs should not be used to treat acute grief reactions as they
91 interfere with the normal grieving process.

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93 10. Patients receiving a new prescription for a BZD for anxiety will be
94 advised on nondrug therapies. Counseling referral will be strongly
95 recommended.

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97 11. Prescription BZDs are often diverted. Care should be taken when
98 prescribing to reduce the risk of diversion.

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100 12. This section deals with the patient already on long-term BZDs. There is
101 no evidence supporting the long-term use of BZDs for any mental health
102 indication. At the time of BZD prescription renewal or medication review,
103 the physician should discuss the risks of long-term BZDs and the benefits of
104 discontinuation (on cognition, mood, sleep, and energy level) and advise the
105 patient to reduce or discontinue the BZD. For some patients this will be
106 difficult or impossible, but the effort should be made. For some a reduction
107 in dose, rather than discontinuation, will be the goal.

108 Those willing to taper their BZDs or hypnotics should attempt a taper of
109 their current BZD or hypnotic. The taper should be slow—starting with ½
110 of a tablet every 2 weeks (or 10 to 12% of the daily dose if the BZD is taken

111 once daily). Exceptions to this are zolpidem and zaleplon, which may be
112 tapered more quickly or even stopped abruptly since their half-life is so
113 short. Eszopiclone has a half-life in the range of short-acting BZDs (6 hrs)
114 so will need to be tapered as are other BZDs.

115 The patient should direct the taper as much as is feasible. Some may
116 accomplish this with limited physician input. Others may need a more
117 structured framework of periodic physician visits. Still others will be more
118 comfortable having the physician closely supervise the tapering schedule.
119 The rate of tapering should be individualized. The process may take 3 to 12
120 months to complete.

121 If this is not successful or if the patient and physician prefer, they can be
122 switched to an equivalent dose of a long-acting BZD (diazepam or
123 chlordiazepoxide) and tapered off that. If a switch is made, it should be
124 stepwise—one dose every one to two weeks if the patient is on multiple
125 daily doses—and should be completed before tapering begins. See the table
126 below for dose equivalents that may be used in this conversion.

127 Counseling should be available to assist with the withdrawal process. The
128 counselor may be utilized to treat the underlying condition for which the
129 BZD was prescribed, to address personal crises which may derail the
130 tapering schedule, and to deal with rebound anxiety.

131 For a more detailed discussion of how to withdraw patients from BZDs,
132 consult the references below, including the website *www.benzo.org.uk*

134 13. Special Considerations

- 135 a) Care should be taken not to taper alprazolam too rapidly, nor to
136 switch from it to another BZD too abruptly, as withdrawal seizures
137 are more prone to occur with it than with other BZDs.
- 138 b) Patients who have previous addiction problems, are on high doses
139 of BZDs, or who are taking opiates or amphetamines concurrently
140 will be more difficult to withdraw and may benefit from referral to
141 an addiction specialist.
- 142 c) Remember that as patients become elderly they will become more
143 sensitive to the same dose of a BZD and have higher risks of
144 adverse effects, so patients who are not able to stop long-term
145 BZDs should at least have their dose reduced as they age.

149 **EQUIVALENCE TABLE TO BE USED FOR**
150 **SUBSTITUTION DURING WITHDRAWAL**

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152	Alprazolam (Xanax)	0.5 mg
153	Chlordiazepoxide (Librium)	25 mg
154	Clonazepam (Klonopin)	0.5 mg
155	Diazepam (Valium)	10 mg
156	Lorazepam (Ativan)	1 mg
157	Temazepam (Restoril)	20 mg
158	Zolpidem (Ambien)	20 mg
159	Zaleplon (Sonata)	20 mg
160	Eszopiclone (Lunesta)	3 mg

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164 **BIBLIOGRAPHY FOR MAINE BENZODIAZEPINE**
165 **GUIDELINES**

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167 **PUBLISHED GUIDELINES**

168
169 www.state.ky.us/agencies/kbml/policy/benzo.pdf

170 A succinct and practical guideline from the Kentucky Medical Licensing Board

171
172 www.racgp.org.au/guidelines/benzodiazepines/

173 Guidelines from Australia

174
175 www.le.ac.uk/cgrdu/benzo-ct17.pdf

176 This site contains a set of audit criteria for appropriate benzodiazepine use

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178 www.benzo.org.uk

179 Large site that is consumer-oriented, but of interest to clinicians also. Useful information
180 on BZD withdrawal, links to other sites.

181 See the page “Benzodiazepines around the world”.

182
183 www.nice.org.uk

184 This site contains a guideline for anxiety disorders that is long and comprehensive. It
185 comes with an extensive, up-to-date bibliography.

186
187 www.dohc.ie/publications

188 Department of Health and Children (Ireland) August 2002
189 Report of the Benzodiazepine Committee
190
191 www.uptodate.com
192 This widely used reference, available by paid subscription, dicusses recommended
193 evaluation and treatment of common mental health diagnoses
194
195 Ashton, Heather
196 Guidelines for the rational use of benzodiazepines
197 *Drugs* 1994; 48(1)
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199 Australian and New Zealand clinical practice guidelines for the treatment of panic
200 disorder and agoraphobia
201 *Australian and New Zealand Journal of Psychiatry* 2003; 37:641-656
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203 Guidelines for the prevention and treatment of benzodiazepine dependence: Summary of
204 a report from the Mental Health Foundation (UK)
205 *Addiction* (1993) 88, 1707-1708
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207 Muller JE et al
208 Social anxiety disorder: current treatment recommendations
209 *CNS Drugs* 2005; 19(5): 377-91
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211 Van Ameringen M et al
212 World Council of Anxiety recommendations for the long-term treatment of social phobia
213 *CNS Spectrum* 2003; Aug 8 (8 SUPPL 1) 40-52
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215 Pollack MH et al
216 World Council of Anxiety recommendations for the long-term treatment of panic
217 disorder
218 *CNS Spectrum* 2003; Aug 8 (8 SUPPL 1) 17-30
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221 **REVIEWS AND META-ANALYSES**

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223 Treatment of Insomnia
224 *CJAM* 2000; 16, 162920: 211-225
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226 Van Lalkom AJ, Bakker A, Spinhover P, et al
227 A meta-analysis of the treatment of panic disorder with or without agoraphobia: a
228 comparison of psychopharmacological, congitive-behavioral, and combination treatments
229 *Journal of Nervous and Mental Disease* 1997; 185: 8.510-516
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231 Bakker A, van Balkom AJ, Spinhoven P et al
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233 review
234 *Journal of Nervous and Mental Disease* 1998;186:7.414-419
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236 Otto MW et al
237 Empirically supported treatments for panic disorder: costs, benefits and stepped care
238 *Journal of Consulting and Clinical Psychology* 2000; 68: 556-563
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240 Gould RA, Otto MW, Pollack MH, et al
241 Cognitive behavioral and pharmacological treatment of generalized anxiety disorder: a
242 preliminary meta-analysis
243 *Behavior Therapy* 1997; 28: 285-305
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245 Roerig JL
246 Diagnosis and management of generalized anxiety disorder
247 *Journal of the American Pharmaceutical Association* 1999; 39: 6.811-821
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249 Davidson JRT, Ballenger JC, Lecrubier Y, et al
250 Pharmacotherapy of generalized anxiety disorder
251 *Journal of Clinical Psychiatry* 2001; 62: SUPPL. 11: 46-52
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253 Barker MJ
254 Cognitive effects of long-term benzodiazepine use: a meta-analysis
255 *CNS Drugs* 2004; 18(1): 37-48
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257 Furukawa TA et al
258 Antidepressants and benzodiazepines for major depression
259 *Cochrane Database Syst Rev* 2001; 2: CD 001026
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261 Cummings RG, LeCouteur DG
262 Benzodiazepines and the risk of hip fracture in older people: a review of the evidence
263 *CNS Drugs* 2003; 17(11); 825-837
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266 An overview of generalized anxiety disorder disease state: appropriate therapy
267 *Clinical Ther* 2000: 22 SUPPL A: A3-19
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269 Wagstaff AJ et al
270 Paroxetine- an update of its use in psychiatric disorders in adults
271 *Drugs* 2002; 62: 4.655-703
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274 Optimizing Pharmacotherapy of generalized anxiety disorder to achieve remission
275 *Journal of Clinical Psychiatry* 2001; 62 SUPPL 19: 20-25

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277 Butler AC, Chapman JE, Forman EM, Beck A
278 The empirical status of cognitive-behavioral therapy: a review of meta-analyses
279 *Clin Psychol Rev* 2005 Sept 29 (in press)

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282 **RELEVANT STUDIES**

283

284 Below are a few recent studies involving outcomes of long-term benzodiazepine therapy,
285 issues around discontinuation, combining benzodiazepines with psychological therapies,
286 and other studies that are unique and relevant. A review of Medline reveals numerous
287 studies addressing short-term use of benzodiazepines in various mental health disorders
288 and as muscle relaxants, cognitive effects of benzodiazepines, other problems with
289 benzodiazepines in geriatric patients, and effects of benzodiazepines on driving and
290 injury risk, which will not be listed here.

291

292 Power KG

293 A controlled comparison of cognitive-behavior therapy, diazepam, and placebo. Alone
294 and in combination, for the treatment of generalized anxiety disorder
295 *Journal of Anxiety Disorders* 1990; 4; 4:267-292 Vashaar RC et al

296

297 Alprazolam revisited

298 *Medical Letter of Drugs and Therapeutics* 2005 Jan 17; 47(1208): 5-7

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300 Zolpidem is not superior to temazepam with respect to rebound insomnia: a controlled
301 study

302 *European Neuropsychopharmacology* 2004 Aug; 14(4): 301-306

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304 The following studies examine the negative influence of benzodiazepines on
305 psychological therapies, particularly when used on an as-needed basis.

306

307 Van Balkom AJ, de Beurs E, Loele P, et al

308 Long-term benzodiazepine use is associated with smaller treatment gain in panic disorder
309 with agoraphobia

310 *Journal of Nervous and Mental Disease* 1997; 185: 8:510-516

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312 Westra HA, Stewart SH, Conrad BE

313 Naturalistic manner of benzodiazepine use and cognitive behavioral therapy outcome in
314 panic disorder with agoraphobia

315 *Journal of Anxiety Disorders* 2002; 16: 3:233-246

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317 In this study of diazepam vs. placebo for GAD demonstrating only short-term benefit
318 from diazepam, the diazepam group doesn't suddenly worsen after 3 weeks, but rather

4/18/2006

319 the placebo group catches up.

320

321 Pourmotabbed T, McLeod DR, et al

322 Treatment, discontinuation, and psychomotor effects of diazepam in women with

323 generalized anxiety disorder

324 *Journal of Clinical Psychopharmacology* 1996; 16: 202-297 Reference ID: 70

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326 This study suggests that benzodiazepines increase the risk of relapse in the alcoholic.

327

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329 Low-dose diazepam primes motivation for alcohol and alcohol-related semantic networks

330 in problem drinkers

331 *Behavioral Pharmacology* 2004 Nov; 15(7): 503-512

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333 The following studies address outcomes of benzodiazepine discontinuation:

334

335 Vorma H et al

336 Long-term outcome after benzodiazepine withdrawal treatment in subjects with

337 complicated dependence

338 *Drug and Alcohol Dependence* 2003 June 5; 70(3): 309-315

339

340 Morin CM et al

341 Long-term outcome after discontinuation of benzodiazepines for insomnia

342 *Behav Res Ther* 2005 Jan; 43(1) 1-14

343

344 Oconnor KP et al

345 Psychological distress and adaptational problems associated with benzodiazepine

346 withdrawal

347 *Addict Behav* 2004 May 29; (8) 583-593

348

349 Connor KM et al

350 Discontinuation of clonazepam in the treatment of social phobia

351 *Journal of Clinical Psychopharmacology* 1998 Oct 18(5); 373-378

352

353

354 These studies examine the long-term prognoses of anxiety disorders and the long-term

355 outcomes of various treatments.

356 Adersch S, Hetta J

357 A 15-year followup study of patients with panic disorder

358 *European Psychiatry* 2003 Dec; 18(8): 401-408

359

360 Swoboda H, Amering M, et al

361 The long-term course of panic disorder—an 11-year follow-up

362 *Journal of Anxiety Disorders* 2003; 17(2): 223-232

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4/18/2006

364 Durham RC, Chambers JA, MacDonald RR et al
365 Does cognitive-behavioural therapy influence the long-term outcome of generalized
366 anxiety disorder? An 8-14 year follow-up of two clinical trials
367 *Psychological Medicine* 2003; 33: 499-509
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