
















Name Generic -TRADE	Equivalent Dose/Class	Peak Level/ ABSORPTION RATE	Average Half-life (hr)	Active Metabolites	Comments (√ = therapeutic use)	INITIAL & MAX DOSE	USUAL DOSE RANGE	\$  /Month
SHORT ACTING: more rebound anxiety effect & withdrawal reactions, better sedative/hypnotic; preferred over long acting in elderly (less accumulation) & in patients with liver disorders (easier metabolized)								
Alprazolam -XANAX (0.25 ⁵ , 0.5 ⁵); (1 ⁵ mg tab; TS 2 ⁵ mg)* [▼]	 0.5mg Pregnancy ←category Triazololo	1-2 hr <i>Medium</i>	12 (9-20)	Minor Oxidation #	√Anxiety, Panic attacks Severe withdrawal & some ? antidepressant effect DI's: Level ↑ by: diltiazem, Luvox, ketoconazole, grapefruit juice, nefazodone, Prozac, ritonavir; ↓ by: theophylline.	0.25mg 4-10mg	0.25mg po tid 0.5mg po tid	16 17
Bromazepam -LECTOPAM (1.5 ⁵ , 3 ⁵ , 6 ⁵ mg tab)	 3mg 2-Keto	1-4 hr <i>Medium</i>	20 (8-30)	Minor Oxidation	√Anxiety ? May exacerbate depression	3mg 30-60mg	3mg po hs 6mg po hs	11 12
Lorazepam -ATIVAN (0.5, 1 ⁵ , 2 ⁵ mg po tab); (0.5, 1.2mg sl tab*; 4mg/ml )*	 1mg 3-Hydroxy	PO 1-4 hr SL/IM 1 hr IV 5-10 min <i>Medium</i>	15 (8-24)	None Conjugation #	√ Anxiety , Preanesthetic; Other: sedative , muscle relaxant, alcohol withdrawal; acute mania ; Fewer DI's , √Status epilepticus -slower onset but longer duration vs diazepam; IM well absorbed	0.5mg 10mg	0.5mg po tid 1mg po tid 2mg po tid	11 12 14
Oxazepam -SERAX (10 ⁵ , 15 ⁵ , 30 ⁵ mg tab)	 15mg 3-Hydroxy	1-4 hr <i>Medium</i>	8 (3-25)	None Conjugation	√ Anxiety, alcohol withdrawal Other: sedative Less affected by liver dysfunction; Fewer DI's	10mg 120mg	15mg po hs 30mg po hs 30mg po tid	10 11 17
Temazepam -RESTORIL (15, 30mg cap)	 10mg 3-Hydroxy	2-3 hr <i>Medium</i>	11 (3-25)	None Conjugation	√ Sedative/hypnotic ; Other: anxiolytic May delay but not suppress REM sleep Fewer DI's	15mg 60mg	15mg po hs 30mg po hs	12 13
Triazolam -HALCION (0.125 ⁵ , 0.25 ⁵ mg tab)	 0.25mg Triazololo	1-2 hr <i>Rapid</i>	2 (1.5-5)	None Oxidation	√ Sedative/hypnotic; DI's as per alprazolam Behavioral disturbances in elderly Prone to withdrawal / rebound effects	0.125mg 0.5mg	0.125mg po hs 0.25mg po hs	9 10
LONG ACTING: less rebound symptoms; better choice when tapering off of BZs (e.g. clonazepam/diazepam); withdrawal may be delayed 1-2 wk for 2-Keto group; bedtime dose option for hypnotic & anxiolytic effect.								
Chlordiazepoxide  (5, 10, 25mg cap) -LIBRIUM	 25mg 2-Keto	1-4 hr <i>Medium</i>	100	Yes Oxidation	√ Anxiety, preanesthetic, alcohol withdrawal Other: sedation; Slower onset vs diazepam	5mg 200-400mg	25mg po tid 50mg po tid	20 32
Clonazepam -RIVOTRIL (0.25* [▼] ; 0.5 ⁵ , 1, 2 ⁵ mg tab)	 0.25mg Nitro	1-4 hr <i>Rapid</i>	34 (19-60)	None Oxidation & Nitro reduction	√ Anticonvulsant, Panic attack Other: sedative , social phobia, akathisia, acute mania , restless leg syndrome & neuralgic pain .Used for BZ withdrawal	0.25mg 10-20mg	0.5mg po tid 1mg po bid 2mg po tid	16 21 21
Clorazepate -TRANXENE (3.75, 7.5, 15mg cap)	 10mg 2-Keto	0.5-2 hr <i>Rapid</i>	100 Inactive until Metabolized	Yes Oxidation	Hydrolyzed in GI → ↓ clorazepate level by antacids √ Anxiety, panic, alcohol withdrawal, seizures	3.75mg 60-90mg	3.75mg po bid 7.5mg po bid 15mg po bid	13 18 26
Diazepam -VALIUM (2 ⁵ , 5 ⁵ , 10 ⁵ mg tab; 10mg/2ml amp; 5mg/ml rectal gel DIASTAT ®; 10mg/2ml emulsion inj* [®] DIAZEMULS)	 5mg 2-Keto	PO 1-2 hr IM 1hr IV 8 min <i>Rapid</i>	100	Yes Oxidation	√Anxiety, muscle relaxant , seizures, alcohol withdrawal & preanesthetic; Other: sedative Quicker onset & ↓ duration of action vs lorazepam, IM causes pain; Diazemuls® IV better tolerated. Used for BZ withdrawal	2mg 40mg	2mg po tid 5mg po tid 10mg po tid	15 16 16
Flurazepam -DALMANE (15, 30mg cap)	 15mg 2-Keto	0.5-1 hr <i>Rapid</i>	100 (40-250)	Yes Oxidation	√ Sedative/hypnotic; Quick onset but accumulates →hangover →confusion, etc.	15mg 60mg	15mg po hs 30mg po hs	10 11
Nitrazepam -MOGADON (5 ⁵ , 10 ⁵ mg tab)	 2.5mg Nitro	0.5-2 hr <i>Medium</i>	30 (15-48)	None Nitro reduction	√ Sedative/hypnotic, myoclonic seizures	5mg 10mg	5mg po hs 10mg po hs	11 12

Side effects: drowsiness, dizziness, ataxia, **dependence**, CNS depression, disorientation, **psychomotor impairment**, confusion, aggression, excitement, ↑ **fall/fractures**⁷ & **vehicle accidents** in elderly & anterograde **amnesia**.



Tolerance to sedative/hypnotic, muscle relaxant & anticonvulsant, but less **tolerance** for the anxiolytic & antipanic effects. No **cross-tolerance** with buspirone & SSRIS; as well often lacks cross-tolerance with alprazolam.

Benzodiazepine withdrawal: Depends on: duration of therapy, dose, rate of tapering & BZ t½ life; **Onset:** 1-2d with short t½; 3-8d with long t½ BZ's; **S/Sx:** insomnia, nausea/vomiting, twitching, irritability, ↑ anxiety, paresthesias, tinnitus, delirium & seizures. **When D/C BZ:** If Tx >12 weeks taper at a rate of +/-25%/week & consider changing to equivalent dose of clonazepam/diazepam (except alprazolam), cognitive behavioral therapy & taper off the BZ.

Length of therapy: **Anxiety:** use as an adjunct only & re-evaluate q4-6 weeks; **Hypnotic:** not to exceed 4 week. **Caution:** BZ & **clozapine** may lead to marked sedation, ↑ salivation, & rare respiratory arrest.

Drug interactions (DI's): ↑ **CNS depression:** antidepressants, antihistamines, barbiturates, ethanol; Antacids ↓ absorption; ↑ **d BZ levels by:** allopurinol, oral contraceptives, cimetidine, estrogen, erythromycin, fluoxetine, isoniazid, omeprazole, valproic (less DI effect on lorazepam, oxazepam, temazepam, but ↑ effect on 2-Keto BZ); **BZ may ↑ levels of:** digoxin & phenytoin. **BZ levels ↓ d by:** carbamazepine, phenobarbital, rifampin & smoking.

Oxidation is a high-energy metabolic pathway impaired in liver disease & reduced in elderly; whereas **conjugation** to more water soluble glucuronide derivative allows for excretion (less intensive), thus less affected by DI's.

Overdose: safe when taken alone; **Treat:** flumazenil. **Precautions:** hx of substance abuse, sleep apnea, cognitive disorder, renal/hepatic dx, **elderly**, porphyria, CNS depression, myasthenia & **pregnancy** (possible teratogen & can precipitate withdrawal in newborns if used in 3rd trimester). **BZ**=benzodiazepine **DI**=drug interaction **Dx**=disease  t½ average(range) can be ↑↑ in geriatric pts & altered by DI's * Non-formulary in Sask  ↓ dose for renal dysfx c=scored ▼ covered NIHB ©not NIHB

¹ Micromedex 2004

² Nelson J, Chouinard G. Guidelines for the clinical use of benzodiazepines: pharmacokinetics, dependency, rebound and withdrawal. Canadian Society for Clinical Pharmacology. Can J Clin Pharmacol. 1999 Summer;6(2):69-83.

³ Rickels K, DeMartinis N, Rynn M, Mandos L. Pharmacologic strategies for discontinuing benzodiazepine treatment. J Clin Psychopharmacol. 1999 Dec;19(6 Suppl 2):12S-16S.

⁴ Teboul E, Chouinard G. A guide to benzodiazepine selection. Part II: Clinical aspects. Can J Psychiatry. 1991 Feb;36(1):62-73.

⁵ Teboul E, Chouinard G. A guide to benzodiazepine selection. Part I: Pharmacological aspects. Can J Psychiatry. 1990 Nov;35(8):700-10.

⁶ Baillargeon L, Landreville P, Verreault R, Beauchemin JP, Gregoire JP, Morin CM. Discontinuation of benzodiazepines among older insomniac adults treated with cognitive-behavioural therapy combined with gradual tapering: a randomized trial. CMAJ. 2003 Nov 11;169(10):1015-1020.

⁷ Wagner AK, Zhang F, Soumerai SB, Walker AM, Gurwitz JH, Glynn RJ, Ross-Degnan D. Benzodiazepine use and hip fractures in the elderly: who is at greatest risk? Arch Intern Med. 2004 Jul 26;164(14):1567-72.