


Generic	Name -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 (0.25,0.5); (1xmg tab, TS 2xmg)	-XANAX	D 0.5mg Pregnancy ←category Triazololo	1-2 hr Medium	12 (9-20)	Minor Oxidation #	√Anxiety, Panic attacks Severe withdrawal & some ? antidepressant effect DIs: Level ↑ by: diltiazem, Luvox, ketoconazole, grapefruit juice, nefazodone, Prozac, ritonavir; ↓ by: theophylline.	0.25mg 4-10mg	0.25mg po tid 0.5mg po tid	15
									15
Bromazepam (1.5, 3, 6mg tab)	-LECTOPAM	D 3mg 2-Keto	1-4 hr Medium	20 (8-30)	Minor Oxidation	√Anxiety ? May exacerbate depression	3mg 30-60mg	3mg po hs 6mg po hs	10 12
Lorazepam (0.5,1,2mg po tab; 0.5x,1x,2xmg sl tab; 4mg/ml amp*)	-ATIVAN	D 1mg 3-Hydroxy	PO 1-4 hr SL/IM 1 hr IV 5-10 min Medium	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 (10,15,30mg tab)	-SERAX	D 15mg 3-Hydroxy	1-4 hr Medium	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 (15,30mg cap)	-RESTORIL	X 10mg 3-Hydroxy	2-3 hr Medium	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	11
									11
Triazolam (0.125,0.25mg tab)	-HALCION	X 0.25mg Triazololo	1-2 hr Rapid	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	D 25mg 2-Keto	1-4 hr Medium	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 (0.5,1,2mg tab)	-RIVOTRIL	D 0.25mg Nitro	1-4 hr Rapid	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	15
									21
Clorazepate (3.75,7.5,15mg cap)	-TRANXENE	D 10mg 2-Keto	0.5-2 hr Rapid	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
Diazepam (2.5,10mg tab; 10mg/2ml amp; 5mg/ml rectal gel; 10mg/2ml emulsion inj* DIAZEMULS)	-VALIUM	D 5mg 2-Keto	PO 1-2 hr IM 1hr IV 8 min Rapid	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
									17
Flurazepam (15,30mg cap)	-DALMANE	X 15mg 2-Keto	0.5-1 hr Rapid	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 (5,10mg tab)	-MOGADON	U 2.5mg Nitro	0.5-2 hr Medium	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, ↑ falls & 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 & the 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 & even 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) & then 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 (DIs): ↑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 DIs.
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 patients & altered by drug interactions * Non-formulary in Sask

¹ Micromedex 2003

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.