PHARMACOKINETIC PROPERTIES OF BENZODIAZEPINES

This table summarizes pharmacokinetic properties of BZD that are important to consider in determining relative risk for physical withdrawal and planning tapering strategies.

Pharmacokinetic Properties of Benzodiazepines[1]

Benzodiazepine	Time to Peak Plasma Level (h; via oral)	Relative Lipid Solubility*	Onset of Action (min)**	Elimination Half-Life (h)†	Metabolism‡
Alprazolam	1–2 h (tablet or ODT) 5–11 h XR	Moderate	15–30	6–12	CYP3A4
Chlordiazepoxide	0.5–4 h	Moderate	15–30	5–10 36–200 (AM)	CYP3A4
Clonazepam	1–2 h	Low	15–30	18–50	CYP3A4
Clorazepate§	0.5–2 h	High	15		CYP2C19 CYP3A4
Diazepam	0.5–2 h	High	≤15	20–100 36–200 (AM)	CYP1A2 CYP2C9 CYP2C19 CYP3A4
Estazolam	2 h	Low	30–60	10–24	CYP3A4
Flurazepam	0.5–2 h	High	≤15	40–250 (AM)	CYP2C19 CYP3A4
Lorazepam	2–4 h	Moderate	15–30	10–20	Glucuronide conjugation
Oxazepam	2–4 h	Low	30–60	4–15	Glucuronide conjugation
Quazepam[2]	2 h	High	15	39 73 (AM)	CYP2C9 CYP2C19 CYP3A4
Temazepam	2–3 h	Moderate	30–60	10–20	Glucuronide conjugation
Triazolam	1–2 h	Moderate	15–30	1.5–5	CYP3A4

This table outlines pharmacokinetic properties of various BZD medications, including the time to peak plasma level following oral administration, relative lipid solubility, onset of action, elimination half-life of the active metabolite, and metabolism.

AM: active metabolite; **ODT:** orally disintegrating tablet; **XR:** extended release

* Increased lipid solubility results in more rapid onset of CNS activity but can also result in rapid redistribution into adipose tissue resulting in a shorter duration of action even in agents with long elimination half-life (eg, diazepam)

**Rapid onset of action is associated with high lipid solubility and increased potential for misuse.

† Agents with moderate to high lipid solubility will have shorter duration of action with single or intermittent doses than suggested by the elimination half-life as these medications distribute rapidly into adipose tissue. With initial dosing, multiple daily doses may be needed to maintain effect. With chronic use and repeated dosing, accumulation is more likely to occur with these agents, especially those with long elimination half-lives (eg, diazepam).[3]

‡ Agents metabolized via glucuronide conjugation do not have pharmacokinetic interactions and are considered to be safer in older adults and patients with hepatic impairment.

§ Hydrolized to nordiazepam in the stomach.

Sources

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2. Aronson JK ed. *Meyler's Side Effects of Drugs. The International Encyclopedia of Adverse Drug Reactions and Interactions*. 16th ed. Elsevier; 2016.

3. Dettli L. Benzodiazepines in the treatment of sleep disorders: pharmacokinetic aspects. *Acta Psychiatr Scand Suppl*. 1986;332:9-19. doi:10.1111/j.1600-0447.1986.tb08975.x