CalOptima Health

Pharmacy Update
June 2025

Risks of Co-prescribing Opioids and Benzodiazepines

According to statistics from the National Institute on Drug Abuse, approximately 14% of overdose deaths caused by opioids also involved the use of benzodiazepines (BZDs).[1] The Centers for Medicare and Medicaid Services (CMS) has introduced a new STAR Ratings measure evaluating the percentage of Part D beneficiaries who have concurrent opioid and BZD claims for at least 30 cumulative days.[2] Many studies have highlighted the dangers of co-prescribing opioids and BZDs due to their additive adverse effects and potential to cause profound sedation, respiratory depression, coma and death. Opioids and BZDs now have FDA boxed warnings in their prescribing information highlighting the potential dangers of using them together. In 2022, the Centers for Disease Control and Prevention (CDC) released updated opioid practice guidelines, which recommended avoiding concomitant BZD and opioid use.[3]

The CDC practice guidelines recommend the following:[3]

- Nonpharmacologic and nonopioid therapies should be maximized prior to opioid initiation.
- Avoid co-prescribing opioids with BZDs. Check CURES (Controlled Substance Utilization Review and Evaluation System) before providing new prescriptions.
- Offer BZD alternatives to patients receiving opioids who require treatment for anxiety, panic disorder, post-traumatic stress disorder or insomnia (Table 1).
- Taper medications if the risks of concomitant use outweigh the benefits:
    - Reduce BZD dose gradually by 25% every one to two weeks.
    - Reduce opioid dose by 10% of starting dose monthly for treatment duration over one year.
    - Reduce opioid dose by 10% of starting dose weekly for treatment duration less than a year.
- Offer naloxone if concurrent opioid and BZD use is necessary.
- Monitor closely for signs of respiratory depression.

Table 1. Medi-Cal Rx and OneCare Formulary BZD Alternatives.

Indication	Generic (Brand)	Recommended Initial Dosing[4]
Generalized Anxiety Disorder	buspirone (Buspar)	7.5 mg twice daily; max 60 mg/day
	duloxetine (Cymbalta)	30–60 mg once daily; max 120 mg/day
	escitalopram (Lexapro)^	10 mg once daily; max 20 mg/day
	mirtazapine (Remeron)^+†	30–60 mg once daily; max 60 mg/day
	paroxetine (Paxil)^+*	20 mg once daily; max 20 mg/day
	sertraline (Zoloft)^+†	25 mg once daily; max 200 mg/day
	venlafaxine ER capsules (Effexor XR) ^+	37.5–75 mg once daily; max 225 mg/day
Insomnia	mirtazapine (Remeron)^†‡	15 mg once daily; max 45 mg/day
	ramelteon (Rozerem)	8 mg once daily at bedtime; max 8 mg/day
	trazodone (Desyrel)†	50–100 mg once daily at bedtime; max 100 mg/day

^Indication or off-label indication for panic disorder; +Indication or off-label indication for PTSD; *High risk medication in older adults age 65 and above; †Off-label indication; ‡For adults with insomnia secondary to comorbid dysthymia

References

1. National Institute on Drug Abuse (NIH). Benzodiazepines and Opioids. Updated November 2022. https://nida.nih.gov/research-topics/opioids/benzodiazepines-opioids. Accessed April 2025.
2. Medicare 2025 Part C & D Display Measure Technical Notes - Measure: DMD10 – Concurrent Use of Opioids and Benzodiazepines (COB). Centers for Medicare and Medicaid Services. Updated December 2024. Accessed April 2025.
3. Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.
4. IBM Micromedex Solutions. Truven Health Analytics Inc. http://micromedex.com. Accessed April 2025.