

Deprescribing Benzodiazepines in Patients Receiving Opioids

According to the Centers for Disease Control and Prevention (CDC), approximately 130 Americans die every day from an opioid overdose, and nearly 30% of the overdoses involve benzodiazepines.¹⁻² The elevated risk of overdose in those concurrently using opioids and benzodiazepines was demonstrated in a 2018 cohort study, which showed that overdose risk was highest in the first 90 days and five times greater than that of those using opioids alone.³ Many studies have highlighted the dangers of co-prescribing opioids and benzodiazepines due to their additive adverse effects and potential for causing profound sedation, respiratory depression, coma, and death.⁴ In addition to the FDA *Boxed Warning*, the CDC issued the *Guideline for Prescribing Opioids for Chronic Pain* in 2016 that recommends clinicians to avoid prescribing benzodiazepines concurrently with opioids whenever possible in the management of chronic non-cancer pain.^{4,5}

The CDC guideline recommends the following⁵:

- Clinicians should taper benzodiazepines gradually since abrupt withdrawal can elicit rebound anxiety, hallucinations, seizures, and delirium tremens.
- A tapering regimen with reduction of the benzodiazepine dose by 25% every 1 to 2 weeks has been used safely and with moderate success. Cognitive behavioral therapy (CBT) increases tapering success rates and might be helpful for patients struggling with the taper.
- Offer evidence-based psychotherapies (e.g., CBT), antidepressants, or other nonbenzodiazepine medications in patients receiving opioids that require treatment for anxiety or insomnia (Table 1).

Table 1. Formulary antidepressants and nonbenzodiazepines for respective indications

Indication	Generic (Brand)	Dosing ⁶	MCAL ^A	OC/OCC ^A
Generalized Anxiety Disorder	citalopram (Celexa)	10-40 mg once daily	Formulary	Formulary
	escitalopram (Lexapro)	10-20 mg once daily	Formulary	Formulary
	paroxetine (Paxil)	20 mg once daily	Formulary [%]	Formulary [%]
	sertraline (Zoloft)	Initial 25-50 mg once daily for 1 week; may titrate up to 200 mg/day	Formulary	Formulary
	duloxetine (Cymbalta)	Initial 30-60 mg once daily; may titrate up to 120 mg/day	Formulary	Formulary
	venlafaxine ER capsules (Effexor XR)	Initial 37.5-75 mg once daily; may titrate up to 225 mg/day	Formulary	Formulary
	buspirone (Buspar)	Initial 7.5 mg twice daily; may titrate up to 60 mg/day	Formulary	Formulary
Insomnia	trazodone (Desyrel)	50-100 mg once daily at bedtime	Formulary	Formulary
	mirtazapine (Remeron)*	15-45 mg daily at bedtime	Formulary	Formulary
	diphenhydramine	25-50 mg at bedtime, for occasional use	Formulary [%]	Formulary [%]

^AMCAL=MediCal; OC=OneCare; OCC=OneCare Connect

*Insomnia with concomitant depression

[%]Prior authorization required for patients age 65 and older

References

1. Centers for Disease Control and Prevention (CDC). Opioid Basics: Understanding the Epidemic. December 19, 2018. Retrieved from <https://www.cdc.gov/drugoverdose/epidemic/index.html>. Accessed on January 8, 2019.
2. National Institute on Drug Abuse (NIH). Benzodiazepines and Opioids. March 2018. Retrieved from <https://www.drugabuse.gov/drugs-abuse/opioids/benzodiazepines-opioids#Reference>. Accessed on January 8, 2019.
3. Hernandez I, He M, Brooks MM, Zhang Y. Exposure-response association between concurrent opioid and benzodiazepine use and risk of opioid-related overdose in Medicare Part D beneficiaries. *JAMA Network Open*. 2018;1(2):e180919.
4. U.S. Food and Drug Administration. Drug Safety Communications: FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning. August 31, 2016. Retrieved from <http://www.fda.gov/downloads/Drugs/DrugSafety/UCM518672.pdf>. Accessed on January 8, 2019.
5. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain--United States, 2016. *JAMA*. 2016;315(15):1624-45.
6. Lexi-Comp, Inc. (Lexi-Drugs®). Lexi-Comp, Inc.; January 8, 2019.

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