CalOptima Health

Pharmacy Update
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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 & Medicaid Services (CMS) has introduced a Star ratings measure evaluating the percentage of Part D beneficiaries with 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 have FDA boxed warnings in their prescribing information highlighting the potential dangers of concomitant use. In 2022, the Centers for Disease Control and Prevention (CDC) released updated opioid practice guidelines, which recommend using particular caution when prescribing BZD and opioids together.[3] The CDC and American Society of Addiction Medicine (ASAM) clinical guidelines recommend the following:[3,4]

- Optimize nonpharmacologic and nonopioid therapies prior to opioid initiation.
- Check the Controlled Substance Utilization Review and Evaluation System (CURES) 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 5 to 25% every 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[5]
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

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