Pharmacy Update August 2019

FDA Adds Boxed Warning to Sedative Hypnotics

In 2018, nearly 30 million prescriptions were dispensed in the United States for sedative hypnotics such as zolpidem (Ambien, Ambien CR, Edluar, Intermezzo, Zolpimist), eszopiclone (Lunesta), and zaleplon (Sonata) for almost 6 million patients. In April 2019, the FDA added a *Boxed Warning* to the labels of these medications, also known as Z-drugs, due to the risk of serious injuries caused by complex sleep behaviors such as sleepwalking, sleep driving, or engaging in other activities while not fully awake. In addition, Z-drugs are now **contraindicated** in patients who have previously experienced an episode of complex sleep behavior with eszopiclone, zaleplon, or zolpidem.[1]

According to the FDA Adverse Event Reporting System (FAERS) database and medical literature, 66 cases of complex sleeping behaviors resulting in serious injuries or death were reported in patients taking eszopiclone, zaleplon, or zolpidem in the United States between December 1992 and March 2018. Twenty of the 66 cases resulted in fatalities, and patients who survived usually did not remember these events. Injuries included:[1]

- Falls
- Accidental overdoses
- Hypothermia
- Apparent suicide attempts
- Motor vehicle collisions

These behaviors have occurred even in patients taking the lowest recommended doses and without a history of complex sleep behaviors. They can also occur when the Z-drugs are taken without alcohol or other sedating medications.[1]

Please note the following FDA recommendations regarding Z-drugs:[1]

- Avoid prescribing eszopiclone, zaleplon, or zolpidem to patients who have previously experienced complex sleep behaviors after taking any of these medications
- When starting patients on Z-drugs, prescribe the lowest recommended dose
- Counsel your patients who are taking these medicines to discontinue them if they experience a complex sleep behavior, even if it did not result in a serious injury
- Advise patients that complex sleep behaviors can occur upon treatment initiation as well as after a longer treatment period

Formulary alternatives for insomnia:[2-3]

Generic (Brand)	Dosing	Medi-Cal	OneCare/OneCare Connect
ramelteon (Rozerem)*	8 mg at bedtime	Prior Authorization Required	Prior Authorization Required for <60 years old
mirtazapine (Remeron)*^	15-45 mg at bedtime	Formulary	Formulary
trazodone (Desyrel)	50-100 mg at bedtime	Formulary	Formulary

*Recommended for elderly patients
^For insomnia with concomitant depression

References

1. U.S. Food and Drug Administration. Drug Safety Communications: FDA adds Boxed Warning for risk of serious injuries caused by sleepwalking with certain prescription insomnia medicines. April 30, 2019. Available at: https://www.fda.gov/media/123819/download
2. Satea M, Buysse D, Krystal A, et al. Clinical practice guideline for the pharmacologic treatment of chronic insomnia in adults: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2017; 13(2):307-349,
3. Lexi-comp, Inc. (Lexidrugs®). Lexi-Comp, Inc.; 2019.

Medi-Cal Educational Bulletins are available through the CalOptima website at www.caloptima.org: Providers-Medi-Cal Pharmacy Resources

The CalOptima Approved Drug List is available on our website: www.caloptima.org
and for PDA download at www.epocrates.com