September Pharmacy Newsletter



An Overview of "Z" Drugs

The "Z-Drugs" are non-benzodiazepine sedative-hypnotics that are FDA approved for the treatment of insomnia in adults. The Z-drugs selectively bind to the certain subunits of the GABA-A complex which allow for hypnotic effects but lack of myorelaxant, anxiolytic, and anticonvulsant effects seen with benzodiazepines.

The three agents in the Z-Drugs group and their approved indications for use are listed below:

- Zolpidem (Ambien) indicated for short-term treatment of insomnia characterized by difficulties with sleep initiation.
- Zaleplon (Sonata) indicated for the short-term treatment of insomnia.
- Eszopiclone (Lunesta) indicated for the treatment of insomnia. The only Z-drug with an approval for long-term/chronic treatment use.

Clinical Considerations with Z-Drugs

The primary areas of concern with members chronically utilizing Z-drugs stems from the drug's highabuse potential and the risk for developing tolerance and dependence. Z-drugs were developed to serve as alternatives to benzodiazepines but should not be considered "safer" than benzodiazepines. Additionally, Z-drugs are listed on the Beers Criteria and are "high-risk" medications for geriatric members. In real-world practice, Z-drugs are overprescribed and used for longer-than-recommended treatment cycles which can put members at a higher risk for developing tolerance, dependence, and adverse effects.

The following points should be taken into consideration when Z-drug therapy may be initiated:

- Studies have shown that the Z-drugs have an abuse potential similar to benzodiazepine and benzodiazepine-like hypnotics.
- If therapy is continued for more than two weeks, the possibility of withdrawal syndrome should be considered, and abrupt discontinuation of therapy avoided.
- Following rapid dose decrease or abrupt discontinuation of the use of sedative-hypnotics there
 have been reports of signs and symptoms like those associated with withdrawal from other CNSdepressant drugs.
- With the possibility of physical and psychological dependence to any of the Z-drugs, these medications require close monitoring.
- Z-drugs should be used cautiously in patients with a history of alcoholism or substance abuse.
- Examples of risks associated with Z-drug use include but are not limited to physical dependence, falls, daytime sedation, and cognitive impairment.
- Sleep studies have shown that Z-drug treatment period should not exceed two weeks as sleep patterns will return to pre-treatment levels after a few weeks of regular use.

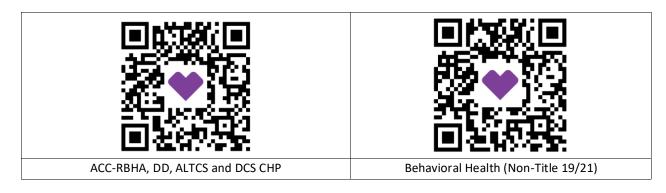
In summary, Z-drugs are approved for use to treat insomnia in adults. The Z-drugs have a high-abuse potential and exert sedative-hypnotic effects that we similarly see with benzodiazepines. To promote responsible prescribing patterns, it is important for providers to consider the clinical benefits and risks associated with Z-drug treatment. Sleep studies have shown that Z-drug treatment period should not

exceed 2 weeks as sleep patterns will return to pre-treatment levels after a few weeks of regular use. Due to the associated risks and reduced long-term efficacy, it is recommended to deprescribe by tapering and eventually discontinuing the Z-drugs whenever possible.

References:

- 1. Clinical Pharmacology. Clinicalkey.com. Published 2019. https://www.clinicalkey.com/pharmacology/
- 2. Jr S, Farrell M. Benzodiazepine & Z-Drug (BZRA) Deprescribing Algorithm.; 2019. https://deprescribing.org/wp-content/uploads/2019/03/deprescribing algorithms2019 BZRA vf-locked.pdf
- 3. Benzodiazepine and Z-Drug Safety Guideline. www.kaiserpermanente.org. Published 2022. Accessed July 22, 2024. https://wa.kaiserpermanente.org/static/pdf/public/guidelines/benzo-zdrug.pdf
- 4. HIGHLIGHTS of PRESCRIBING INFORMATION.; 2018. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/021476Orig1s038rplLBL.pdf#page=26
- Sonata ® (Zaleplon) Capsules CIV WARNING: COMPLEX SLEEP BEHAVIORS.
 https://www.accessdata.fda.gov/drugsatfda docs/label/2019/020859s016lbl.pdf#page=21
- 6. HIGHLIGHTS of PRESCRIBING INFORMATION. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/019908s40s044s047lbl.pdf#page=24
- 7. Mokhar A, Kuhn S, Topp J, Dirmaier J, Härter M, Verthein U. Long-term use of benzodiazepines and Z drugs: a qualitative study of patients' and healthcare professionals' perceptions and possible levers for change. BJGP Open. Published online February 19, 2019:bjgpopen18X101626. doi:https://doi.org/10.3399/bjgpopen18X101626

REFERRED DRUG LIST UPDATES CAN BE FOUND HERE:



^{**} Drugs that are not on the formulary will require a PA (prior authorization) request to be submitted**

Reminder for quicker determinations of a Prior Authorization use the ePA link for Our Providers: Please click <u>here to initiate an electronic prior authorization (ePA)</u> request.

This newsletter is brought to you by the Mercy Care Pharmacy Team. For questions, please email Fanny A Musto (MustoF@mercycareaz.org), Denise Volkov (VolkovD@mercycareaz.org) or Trennette Gilbert (ailbert@mercycareaz.org)