UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

PALLIATIVE CARE PHARMACY PHAST PHACT

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Palliative Care Pharmacy Team:

Clinical Pharmacy Specialist:

Jenn Pruskowski, PharmD, BCPS, BCGP, CPE
pruskowskija@upmc.edu

If you have a topic you would like the pharmacy team to answer, please send your suggestions to: pruskowskija@upmc.edu

TODAY'S TOPIC:

What's New in Palliative Care Medications
Drug #2: Lemborexant (Dayvigo®)

Background:

Lemborexant (Dayvigo®) is an orexin/hypocretin receptor antagonist approved for the treatment of insomnia in adults

- Initial US approval: 2019
- Available as: 5mg and 10mg

Importance:

Insomnia is a common symptom for palliative care patients; up to 30% of the population suffers from insomnia. Palliative care provides should be aware of currently approved pharmacological options.

Pharmacology:

MoA:	The neuropeptide orexin regulates wakefulness; inhibiting orexin receptor signaling promotes sleep. Lemborexant has been reported to inhibit the orexin signaling pathway and promote both REM and non-REM sleep. Lemborexant is considered a DORA (dual orexin receptor antagonist).
ADME:	- A: Tmax: 1-3 hours, Cmax is decreased by 23% and Tmax delayed by 2 hours when coadministered with food - M: CYP 3A4 substrate, M10 (active metabolism) - E: T ½: 17 hours
DIs:	- No significant interactions identified (*yet*)

Key: MoA: Mechanism of Action; ADME: Absorption, Distribution, Metabolism, and Excretion; DI: Drug Interaction; Tmax: time until max concentration; T ½: terminal half-life; Cmax: max concentration; AUC: area under the curve

Other Clinical Points:

CIs:	- Hypersensitivity - Narcolepsy
Warnings and Precautions:	- Concomitant use with other drugs to treat insomnia and alcohol - Daytime impairment may occur and persist for up to several days - Driving abilities may be impaired - High risk of falls - Cataplexy-like symptoms and complex sleep disorders - Worsening of insomnia or the emergence of new cognitive or behavioral abnormalities - Compromised respiratory function
Dosing:	Take 5mg immediately prior to bed and with at least 7 hours remaining before planned time of awakening
ADRs:	Most common adverse reactions (≥2%) are somnolence, disturbance in sleep behavior, sleep paralysis, hypnagogic hallucinations and suicidal thoughts.

Key: CI: contraindications; ADRs: adverse drug reactions

The Literature:

- J Clin Sleep Med. 2018 Aug 15; 14(8): 1399–1408.
  An Update on Dual Orexin Receptor Antagonists and Their Potential Role in Insomnia Therapeutics
  - Narrative review
  - "Developed by Eisai, Inc., lemborexant was created from a parent compound that was previously shown in rats to decrease wakefulness and promote NREM sleep, with no effect on REM sleep. Phase II clinical trials have revealed lemborexant's ability to significantly improve mean sleep efficiency compared to placebo groups, including shortening sleep latency, and wake after sleep onset (WASO) in patients with insomnia. Adverse side effects such as somnolence, headache, and sleep paralysis have been reported. In August 2015, Eisai, Inc. and Purdue Pharma agreed to collaboratively develop lemborexant for the commercial market. As of 2018, phase III trials in patients with general insomnia are being conducted, along with a phase II study testing lemborexant in patients with irregular sleep-wake rhythm disorder and dementia"

So… What does this all mean Jenn?

- It appears many DORAs may be coming to the US market soon
- Cost data is not yet available for lemorexant
- UPMC has not yet reviewed lemorexant; see here for the acute insomnia guidelines

CLINICAL PEARL:
Lemorexant was approved in 2019 for insomnia in adults.