PDL NEW DRUG REVIEW

Proprietary Name: Hetlioz®
Common Name: tasimelteon
PDL Category: Sedative Hypnotics Non-Benzodiazepines

Summary

Indications and Usage: For the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24). This is a pregnancy category C medication. The safety and efficacy of use in children have not been established.

Drug Interactions: The concomitant use of Hetlioz® with fluvoxamine or other strong CYP1A2 inhibitors should be avoided due to the potential of large increases in tasimelteon exposure. The concomitant use of Hetlioz® with rifampin or other CYP3A4 inducers should be avoided due to the potential of large decreases in tasimelteon exposure.

Smoking causes induction of CYP1A2 levels. As the exposure of tasimelteon was lower in smokers vs non-smokers, the efficacy of Hetlioz® treatment may be reduced in the smoking population.

The concomitant use of Hetlioz® with beta adrenergic receptor antagonists may reduce the efficacy of Hetlioz®.

Dosage Forms: Capsules: 20mg

Recommended Dosage: Take 20mg per day without food before bedtime, at the same time every night. Drug effects may not occur for weeks or months. Dose adjustments are not needed in patients with mild or moderate hepatic impairment; however, as it has not been studied with severe hepatic impairment, it is not recommended for use in this population. Dosage adjustment is not required in those with renal impairment.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Hetlioz®) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same or that the active drug was less than placebo.* The most frequently reported adverse events included headache (10%), alanine aminotransferase increased (5%), nightmare/abnormal dreams (10%), upper respiratory tract infection (7%), and urinary tract infection (5%).

Hetlioz® can impair the performance of activities needing complete mental alertness. Due to the potential effect of somnolence, it is recommended that after taking Hetlioz®, activities to prepare for going to bed should be limited.

Contraindications: There are currently no contraindications listed with this product.

Manufacturer: Vanda Pharmaceuticals

Analysis: Tasimelteon, the active ingredient of Hetlioz®, is a melatonin receptor agonist. While the exact mechanism of action for use in patients with Non-24 is not known, it does target the melatonin MT1 and MT2 receptors, which are believed to be involved in the control of circadian rhythms. "Non-24 is a chronic circadian rhythm (body clock) disorder in the blind that causes problems with the timing of sleep."[2]

The safety and efficacy of Hetlioz® for the treatment of Non-24 was established in 2 randomized, double-blind, placebo-controlled studies in totally blind patients with Non-24. Study 1 (N=84) compared Hetlioz® to placebo, taken one hour before bedtime for up to 6 months. Study 2 (N=20) was a randomized withdrawal trial to assess efficacy after 12 weeks of use. Efficacy endpoints were nighttime total sleep time and daytime nap duration based on 25% of nights with the least nighttime sleep and 25% of days with most daytime nap time. In Study 1, the baseline average of nighttime sleep was 195 minutes and daytime nap time was 137 minutes on the 25% of most symptomatic nights and days, respectively. Hetlioz® treatment resulted in significant improvement for both of these endpoints as compared with placebo.

In Study 1, the change from baseline in nighttime sleep time on 25% most symptomatic nights was 50 minutes with Hetlioz® vs 22 minutes with placebo; the change from baseline in daytime nap time on 25% most symptomatic days was -49 minutes with Hetlioz® vs -22 minutes with placebo. A responder analysis of subjects with both ≥45 minutes increase in nighttime sleep and ≥45 minutes decrease in daytime nap time was 29% with Hetlioz® vs 12% with placebo.

Study 2 was a randomized withdrawal study to assess the maintenance of efficacy after 12 weeks. The change from baseline in nighttime sleep time on 25% most symptomatic nights was -7 minutes with Hetlioz® vs -74 minues with placebo; the change from baseline in daytime nap time on 25% most symptomatic days was -9 minutes with Hetlioz® vs 50 minutes with placebo.

It is recommended that Hetlioz® remain non-preferred and require clinical prior authorization to verify diagnosis.

PDL Placement:

- ☐ **Preferred**
- ☒ **Non-Preferred**
- ☒ **Refer to DUR for PA Criteria**

References

[1] Hetlioz [package insert]. Washington, D.C.; Vanda Pharmaceuticals, Inc; 2014.

[2] FDA News Release. FDA approves Hetlioz®: first treatment for non-24 hour sleep-wake disorder in blind individuals. Website: http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm384092.htm. Accessed May 2014.