Sunosi™ (solriamfetol) – New orphan drug approval

- On March 20, 2019, Jazz Pharmaceuticals announced the FDA approval of Sunosi (solriamfetol), to improve wakefulness in adult patients with excessive daytime sleepiness associated with narcolepsy or obstructive sleep apnea (OSA).
    - Sunosi is not indicated to treat the underlying airway obstruction in OSA. Ensure that the underlying airway obstruction is treated (eg, with continuous positive airway pressure) for at least one month prior to initiating Sunosi for excessive daytime sleepiness. Modalities to treat the underlying airway obstruction should be continued during treatment with Sunosi. Sunosi is not a substitute for these modalities.
    - Sunosi is expected to receive final controlled substance scheduling by the Drug Enforcement Administration (DEA) within the next 90 days.
- Both narcolepsy and OSA are characterized by excessive daytime sleepiness.
    - Narcolepsy affects an estimated one in 2,000 people in the U.S., with symptoms typically appearing in childhood.
    - OSA is prevalent in 14% of men and 5% of women.
- Sunosi's mechanism of action to improve wakefulness in patients with excessive daytime sleepiness associated with narcolepsy or OSA is unclear. However, its efficacy could be mediated through its activity as a dopamine and norepinephrine reuptake inhibitor.
- The efficacy of Sunosi in improving wakefulness and reducing excessive daytime sleepiness was demonstrated in a double-blind study of 239 adult patients with narcolepsy. Patients were randomized to receive Sunosi 75 mg, 150 mg, or 300 mg, or placebo once daily. The co-primary efficacy endpoints were change from baseline in Maintenance of Wakefulness Test (MWT) and Epworth Sleepiness Scale (ESS) at week 12.
    - Patients randomized to Sunosi 150 mg showed statistically significant improvements on the MWT (treatment effect difference: 7.7 minutes [95% CI: 4.0, 11.3]) and on the ESS (treatment effect difference: -3.8 points [95% CI: -5.6, -2.0]) vs. placebo at week 12. The Sunosi 75 mg dose did not reach statistical significance.
- The efficacy of Sunosi in improving wakefulness and reducing excessive daytime sleepiness was demonstrated in a double-blind study of 476 adult patients with OSA. Patients were randomized to receive Sunosi 37.5 mg, 75 mg, 150 mg, or 300 mg, or placebo once daily. The co-primary efficacy endpoints were change from baseline in MWT and ESS at week 12.
    - Patients randomized to Sunosi 37.5 mg, 75 mg, and 150 mg showed statistically significant improvements on the MWT (treatment effect difference: 4.5 minutes, 8.9 minutes, and 10.7 minutes, respectively) and ESS (treatment effect difference: -1.9 points, -1.7 points, and -4.5 points, respectively) vs. placebo at Week 12.
- In addition, the maintenance of effect of Sunosi in improving wakefulness and reducing excessive daytime sleepiness in patients with narcolepsy and OSA was assessed in two placebo-controlled studies. The first study was a 6-week randomized-withdrawal study in 174 patients with OSA. The co-primary efficacy endpoints were change from the beginning to the end of the randomized-withdrawal period in MWT and ESS. The second study was a 52-week, open-label study in 638 patients with either narcolepsy or OSA; patients received stable-dose treatment for 6 months, and

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then entered the randomized-withdrawal period. The primary efficacy endpoint was change from the beginning to the end of the randomized-withdrawal period in ESS.

  - In study 1, patients randomized to placebo experienced statistically significant worsening of sleepiness as measured by the MWT and ESS vs. patients who remained on Sunosi (difference from placebo: 11.2 [95% CI: 7.8, 14.6] and -4.6 [95% CI: -6.4, -2.8], respectively).
  - In study 2, patients randomized to placebo experienced statistically significant worsening of sleepiness as measured by the ESS vs. patients who remained on Sunosi (difference from placebo: -3.7 [95% CI: -4.8, -2.7]).

- Sunosi is contraindicated with concurrent treatment with a monoamine oxidase inhibitor (MAOI) or use of an MAOI within the preceding 14 days.

- Warnings and precautions of Sunosi include blood pressure and heart rate increases, and psychiatric symptoms.

- The most common adverse reactions (≥ 5% and > placebo) with Sunosi use were headache, nausea, decreased appetite, insomnia, and anxiety.

- The recommended starting dose of Sunosi in adults with narcolepsy and OSA is 75 mg orally once daily and 37.5 mg orally once daily, respectively. The recommended dose range for Sunosi is 75 mg to 150 mg once daily and 37.5 mg to 150 mg once daily for narcolepsy and OSA, respectively.

  - Based on efficacy and tolerability, the dosage of Sunosi may be doubled at intervals of at least 3 days.
  - The maximum recommended dose is 150 mg once daily.
  - Dosages above 150 mg daily do not confer increased effectiveness sufficient to outweigh dose-related adverse reactions.
  - Sunosi should be administered orally upon awakening with or without food.
  - Sunosi should not be taken within 9 hours of planned bedtime because of the potential to interfere with sleep if taken too late in the day.

- Jazz Pharmaceuticals plans to launch Sunosi after the DEA assigns the controlled substance scheduling. Sunosi will be available as a scored 75 mg tablet and a 150 mg tablet.