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SUNOSI (solriamfetol) Executive Summary for Medicaid

SUNOSI is a dopamine and norepinephrine reuptake inhibitor (DNRI) indicated to improve wakefulness in adult patients with Excessive Daytime Sleepiness (EDS) associated with narcolepsy or Obstructive Sleep Apnea (OSA). SUNOSI is available in a scored 75mg tablet and in a 150mg tablet. SUNOSI is dosed once daily in the morning, given with or without food. Patients with narcolepsy are initiated on 75mg once daily for 3 days, and then may be titrated up to a maintenance dose of 150mg. Patients with OSA initiate at 37.5 mg and may titrate up to a maximum of 150mg daily. SUNOSI has a CIV designation.
SUNOSI is not indicated to treat the underlying airway obstruction in OSA. Ensure that the underlying airway obstruction is treated (e.g. with continuous positive airway pressure (CPAP)) 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 prescribing information, Jazz Pharmaceuticals, 2019)

Solriamfetol is a wake-promoting agent with a mechanism of action as a selective dopamine and norepinephrine reuptake inhibitor (DNRI) (Baladi et al., 2018). The efficacy of solriamfetol in the treatment of EDS is thought to be mediated through its activity as a DNRI. The mechanism of action of solriamfetol is different from traditional stimulants or wake-promoting agents, such as d-amphetamine, modafinil, and armodafinil. In contrast to amphetamine, solriamfetol does not promote release of norepinephrine (Baladi et al., 2018). Solriamfetol has binding and activity at both the dopamine and norepinephrine transporters (Baladi et al., 2018), whereas it is thought that modafinil exerts its effects predominantly through a dopaminergic mechanism (Wisor, 2013). Solriamfetol does not cause rebound hypersomnia, which occurs with traditional stimulants (Hasan et al., 2009).

Solriamfetol – Efficacy and Safety

Solriamfetol is an oral, once daily medication, with effects seen within one hour, and lasting up to nine hours at doses of 150 mg following 12 weeks of continuous dosing. The solriamfetol phase 3 clinical program included a study evaluating EDS in adult participants with narcolepsy (TONES 2) and two studies evaluating EDS in adult participants with OSA (TONES 3 and TONES 4). An open-label, long-term safety and maintenance of efficacy study (TONES 5) enrolled participants with narcolepsy and participants with OSA, and included a 2-week randomized-withdrawal phase following 6 months of treatment. Solriamfetol efficacy was evaluated as treatment-related changes in the Maintenance of Wakefulness Test (MWT; TONES 2-4) and the Epworth Sleepiness Scale (ESS; TONES 2-5).

The MWT is an objective measure of an individual's ability to remain awake during the daytime in a darkened, quiet environment, with sleep latency (the time taken to fall asleep; in minutes) as the measure; lower sleep latency indicates greater sleepiness (Littner et al., 2005). The ESS is an 8-item patient-reported measure of a person's general level of daytime sleepiness or their average sleep propensity in eight common daily activities; higher scores indicate greater sleepiness, and normal values are ≤10 (Johns, 1991).

The TONES 2 study assessed the safety and efficacy of 75 mg, 150 mg, and 300 mg of solriamfetol in participants with EDS in narcolepsy over a period of 12 weeks (n=236) (Thorpy et al., 2019). The co- primary endpoints of this study were change from baseline to week 12 in MWT mean sleep latency and ESS score. Study results demonstrated that MWT sleep latency was increased by a range of 4.7-12.3 minutes and mean ESS scores were reduced by a range of 3.8-6.4 points with doses of solriamfetol ranging from 75-300 mg. The most commonly reported treatment-emergent adverse events (AEs) across

all doses of solriamfetol (occurring in >5% of participants across all solriamfetol groups) were headache, nausea, decreased appetite, nasopharyngitis, dry mouth, and anxiety (Thorpy et al., 2019).

The TONES 3 study was a 5-arm, parallel-group study evaluating four doses of solriamfetol (37.5 mg, 75 mg, 150 mg and 300 mg) and placebo for a 12-week period in participants with EDS in OSA (n=474) (Schweitzer et al., 2018a). The co-primary endpoints of this study were change from baseline to week 12 in MWT mean sleep latency and ESS score. Study results demonstrated that MWT sleep latency was increased by a range of 4.7-13.0 minutes (all P <0.05) and mean ESS scores were reduced by a range of 5.0-7.9 points (all P <0.05) with doses of solriamfetol ranging from 37.5-300 mg. AEs reported with solriamfetol (occurring in >5% of participants) were headache, nausea, decreased appetite, anxiety, and nasopharyngitis (Schweitzer et al., 2018a).

The effects of solriamfetol are clinically meaningful. The average MWT sleep latency improved to the range observed in healthy controls (≥19.4 min; Doghramji et al., 1997) at all doses in OSA (Schweitzer et al. 2018a). The wake-promoting effects of the 150 mg dose were evident one hour after dosing and persisted through each of the five MWT trials across the day (spanning a nine hour duration of effect) (Schweitzer et al., 2018b). A high percentage of patients with OSA (52-73%) or narcolepsy (30-49%) treated with solriamfetol reached a normal score on the ESS (≤10) compared with placebo (post-hoc analyses) (Rosenberg et al., 2018).

No studies were performed with an active comparator (head to head studies). There were no clinically meaningful differences in efficacy across all subpopulations defined (age, gender, or race) or other factors (BMI, presence of cataplexy, baseline primary OSA therapy or baseline severity of sleepiness) (Data on file, Jazz Pharmaceuticals, 2018)

Across all solriamfetol studies, the most common AEs (≥5%) were headache, nausea, decreased appetite, anxiety, nasopharyngitis, diarrhea, and dry mouth. Discontinuation rates due to AEs (3%) were low (SUNOSI prescribing information, Jazz Pharmaceuticals, 2019).

Contraindications include concurrent treatment with a monoamine oxidase inhibitor (MAOI) or use of an MAOI within the preceding 14 days. Warnings and precautions include blood pressure and heart rate increases and psychiatric symptoms (SUNOSI prescribing information, Jazz Pharmaceuticals, 2019).

References

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