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Pharmacists' Role in Supporting Patients With Excessive Daytime Sleepiness Associated With Obstructive Sleep Apnea

FEELING TIRED DURING THE DAY is one of the most common complaints from patients with obstructive sleep apnea (OSA),¹ which is a chronic condition that involves total or partial upper airway obstruction during sleep with periodic episodes of hypoxia and sleep disturbance.²

Excessive daytime sleepiness (EDS) associated with OSA can persist even with the use of primary airway therapy such as continuous positive airway pressure (CPAP), which maintains airway patency during sleep and eliminates apneas.³⁻⁵ An example of this was shown in a study of patients with moderate to severe OSA using CPAP (N=174), daytime sleepiness was assessed before and after 3 months of CPAP therapy using the Epworth Sleepiness Scale (ESS), a validated, patient-reported measure of subjective sleepiness.^{3,6} A total of 52% of patients reported feeling sleepy during the day despite any amount of CPAP use (ranging from less than 2 to 7 or more hours per night).³ Of the patients who used their CPAP for 5 or more hours each night, 1 in 3 patients reported feeling sleepy during the day.³

There is a need for additional management options for adult patients with EDS in OSA who have unresolved EDS despite CPAP adherence. As part of the health care team, pharmacists can support with the identification of patients with EDS associated with OSA and help patients understand treatment options available, such as SUNOSI® (solriamfetol), which is part of a comprehensive approach to managing EDS.^{7,8}

SUNOSI® (SOLRIAMFETOL)

SUNOSI is the first and only dopamine-norepinephrine reuptake inhibitor that is indicated to improve wakefulness in adults with EDS associated with OSA.⁸ SUNOSI is not indicated to treat the airway obstruction in OSA. Ensure that the underlying airway obstruction is treated (eg, with CPAP) for at least 1 month prior to initiating SUNOSI for EDS. SUNOSI is not a substitute for these modalities and the treatment of the underlying airway obstruction should be continued.⁸

INDICATIONS AND USAGE

SUNOSI is indicated to improve wakefulness in adults with excessive daytime sleepiness (EDS) associated with narcolepsy or obstructive sleep apnea (OSA).

Limitations of Use:

SUNOSI is not indicated to treat the underlying 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. SUNOSI is not a substitute for these modalities, and the treatment of the underlying airway obstruction should be continued.

SUNOSI is not a traditional stimulant.^{8,9} Although the exact mechanism of action is unclear, SUNOSI is thought to work by selectively inhibiting the reuptake of dopamine and norepinephrine transporters.^{8,9} SUNOSI is contraindicated with concomitant treatment with a monoamine oxidase inhibitor (MAOI) or use of an MAOI within the preceding 14 days.⁸

Pharmacists can support patients who are prescribed SUNOSI; they can prepare to discuss dosing and administration, efficacy, safety, and practical information to support patients with access to their prescription during counseling sessions.

DOSING AND ADMINISTRATION

SUNOSI is available as a once-daily tablet (75 mg and 150 mg for OSA). For adult patients with OSA, SUNOSI is initiated at 37.5 mg and titrated up as needed to 75 mg after 3 days. SUNOSI is titrated up as needed to 150 mg after 3 days. The maximum recommended dosage is 150 mg once daily.⁸

SUNOSI should be taken upon awakening, and at least 9 hours before planned bedtime to avoid potential interference with sleep. SUNOSI can be taken with or without food, and no timing with meals is necessary.⁸

During counseling, pharmacists can review dosing and administration information and the titration schedule for SUNOSI once-daily tablet for patients with OSA.⁸ Reinforce that patients should check with their physician before discontinuing treatment that they perceive as ineffective, as the dose may be modified up to 150 mg for greater efficacy.⁸

CLINICAL EFFICACY

The efficacy and safety profile of SUNOSI for EDS in OSA was explored in a 12-week, randomized, multicenter, double-blind, placebo-controlled, parallel group study in adult patients with OSA (N=459).^{8,10} Entry criteria were an ESS score of 10 or more and a mean sleep latency of less than 30 minutes as documented by the mean of the first 4 trials of the Maintenance of Wakefulness Test (MWT), which measures patients' ability to

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remain awake during the daytime.^{8,10} The study arms included patients that received once-daily SUNOSI® (solriamfetol) 37.5 mg (n=56), 75 mg (n=58), 150 mg (n=116), and 300 mg (n=115; 2 times the maximum recommended daily dose), and placebo (n=114).¹⁰ Coprimary end points were least square (LS) mean change from baseline to week 12 in both the ESS score and mean sleep latency on the MWT.¹⁰

DAYTIME SLEEPINESS (ESS)

At week 12, SUNOSI significantly reduced daytime sleepiness, as measured by the ESS, compared with placebo; LS mean change from baseline in ESS scores for patients randomized to SUNOSI 150 mg, 75 mg, 37.5 mg, were -7.7 ($P < .0001$), -5.0 ($P < .05$), and -5.1 ($P < .05$), respectively, vs -3.3 with placebo.^{8,10} Patients experienced 52% less daytime sleepiness as measured by the ESS while taking SUNOSI 150 mg, 26% reduction with SUNOSI 75 mg, and 25% reduction with SUNOSI 37.5 mg compared with just a 15% reduction with placebo at week 12.^{8,10,11,a}

WAKEFULNESS (MWT)

SUNOSI provided more minutes of wakefulness at week 12 from baseline, as measured by the MWT.^{10,11,b} At week 12, there was a significant increase from baseline in the average time that patients treated with SUNOSI were able to remain awake during the 40-minute MWT trials; the LS mean change from baseline was 11.0 minutes with SUNOSI 150 mg ($P < .0001$), 9.1 minutes with SUNOSI 75 mg ($P < .0001$), and 4.7 minutes with SUNOSI 37.5 mg ($P < .05$) compared with 0.2 minutes with placebo.¹⁰ There was an 82% increase in time awake with SUNOSI 150 mg, 61% with SUNOSI 75 mg, and 23% with SUNOSI 37.5 mg compared with 0% with placebo.^{8,10,11,b}

^aMedian percent change from baseline to week 12 was calculated using last observation carried forward and was not adjusted for covariates used in the primary endpoint.¹¹

^bMedian percent change from baseline to week 12 was calculated using last observation carried forward and was not adjusted for covariates used in the primary endpoint. Seven patients were missing baseline values and were not included in the median percent change from baseline.¹¹

^cData reflects pooled OSA and narcolepsy data for 75 mg, 150 mg, and 300 mg doses on SUNOSI. The maximum recommended dose is 150 mg once daily.^{8,12}

IMPORTANT SAFETY INFORMATION CONTRAINDICATIONS

SUNOSI is contraindicated in patients receiving concomitant treatment with monoamine oxidase inhibitors (MAOIs), or within 14 days following discontinuation of an MAOI, because of the risk of hypertensive reaction.

WARNINGS AND PRECAUTIONS

Blood Pressure and Heart Rate Increases

SUNOSI increases systolic blood pressure, diastolic blood pressure, and heart rate in a dose-dependent fashion. Epidemiological data show that chronic elevations in blood pressure increase the risk of major adverse cardiovascular events (MACE), including stroke, heart attack, and cardiovascular death. The magnitude of the increase in absolute risk is dependent on the increase in blood pressure and the underlying risk of MACE in the population being treated. Many patients with narcolepsy and OSA have multiple risk factors for MACE, including hypertension, diabetes, hyperlipidemia, and high body mass index (BMI).

Assess blood pressure and control hypertension before initiating treatment with SUNOSI. Monitor blood pressure regularly during treatment and treat new-onset hypertension and exacerbations of pre-existing hypertension. Exercise caution when treating patients at higher risk of MACE, particularly patients with known cardiovascular and cerebrovascular disease, pre-existing hypertension, and patients with advanced age. Use caution with other drugs that increase blood pressure and heart rate.

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EDS SYMPTOMS (PGI-C)

The key secondary end point was the percentage of patients who self-reported improvements in EDS from baseline by week 12, which was assessed by the Patient Global Impression of Change (PGI-C) 7-point scale ranging from “very much improved” to “very much worse.” The percentage of patients who improved on the PGI-C included those who reported very much, much, and minimal improvement.¹⁰ Across doses, SUNOSI improved symptoms as measured by the PGI-C. At week 12, 90% of patients reported feeling better with SUNOSI 150 mg, 72% with SUNOSI 75 mg, 55% with SUNOSI 37.5 mg, and 49% with placebo.¹⁰

LONG-TERM MAINTENANCE OF EFFICACY

A long-term maintenance of efficacy and safety study initiated open-label SUNOSI in a subset of adult patients with OSA or narcolepsy who had completed a previous SUNOSI trial.¹² Mean ESS score values were 15.9 for parent baseline in Group A and baseline in the current study for Group B was 16.2.¹² Patients were randomized to either continue to receive SUNOSI maintenance at the dose received in the maintenance phase (n=139) or to receive placebo (n=141).¹² The primary end point was the LS mean change in ESS scores from the beginning to the end of the 2-week randomized withdrawal period.^{8,12,c}

Mean ESS scores at the beginning of the randomized withdrawal were 7.3 with SUNOSI and 7.8 with placebo. At the end of the randomized withdrawal ESS scores were 8.5 in the SUNOSI group vs 12.6 in the placebo group.¹² Significant reductions in daytime sleepiness were maintained after 6 months in patients who remained on SUNOSI vs patients who switched to placebo (LS mean difference -3.7; $P < .0001$).^{8,12,c}

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SAFETY AND TOLERABILITY

SUNOSI® (solriamfetol) offers a well-established safety and tolerability profile. Pharmacists can monitor patients for safety and tolerability with SUNOSI throughout their treatment.

ADVERSE EVENTS

In pooled, 12-week, placebo-controlled OSA and narcolepsy studies, the rate of discontinuation due to adverse reactions (ARs) with SUNOSI was 3% vs less than 1% with placebo.⁸ The most common ARs (incidence $\geq 5\%$ and greater than placebo) reported were headache, nausea, decreased appetite, anxiety, and insomnia.⁸

In OSA studies, the most-common ARs greater or equal to 2%, and greater than placebo, in patients treated with 37.5 mg, 75 mg, and 150 mg SUNOSI (n = 235) vs placebo (n = 118) were nausea and vomiting (8% vs 6%), decreased appetite (6% vs 1%), anxiety (4% vs 1%), and diarrhea (4% vs 1%).⁸

DRUG INTERACTIONS

SUNOSI should not be used concomitantly with MAOIs, drugs that increase blood pressure, heart rate, or dopaminergic drugs. Pharmacokinetic drug interactions are unlikely to occur with SUNOSI. It is not metabolized by the liver and it is not an inhibitor of major metabolizing (CYP) enzymes or renal transporters. It is predominantly excreted unchanged in the urine, undergoes minimal metabolism in humans, and shows low plasma protein binding.⁸

IMPORTANT SAFETY INFORMATION (CONT'D)

Blood Pressure and Heart Rate Increases (Cont'd)

Periodically reassess the need for continued treatment with SUNOSI. If a patient experiences increases in blood pressure or heart rate that cannot be managed with dose reduction of SUNOSI or other appropriate medical intervention, consider discontinuation of SUNOSI.

Patients with moderate or severe renal impairment could be at a higher risk of increases in blood pressure and heart rate because of the prolonged half-life of SUNOSI.

Psychiatric Symptoms

Psychiatric adverse reactions have been observed in clinical trials with SUNOSI, including anxiety, insomnia, and irritability.

Exercise caution when treating patients with SUNOSI who have a history of psychosis or bipolar disorders, as SUNOSI has not been evaluated in these patients.

Patients with moderate or severe renal impairment may be at a higher risk of psychiatric symptoms because of the prolonged half-life of SUNOSI.

Observe SUNOSI patients for the possible emergence or exacerbation of psychiatric symptoms. Consider dose reduction or discontinuation of SUNOSI if psychiatric symptoms develop.

MOST COMMON ADVERSE REACTIONS

The most common adverse reactions (incidence $\geq 5\%$) reported more frequently with the use of SUNOSI than placebo in either narcolepsy or OSA were headache, nausea, decreased appetite, anxiety, and insomnia.

Dose-Dependent Adverse Reactions

In the 12-week placebo-controlled clinical trials that compared doses of 37.5 mg, 75 mg, and 150 mg/day of SUNOSI to placebo, the following adverse reactions were dose-related: headache, nausea, decreased appetite, anxiety, diarrhea, and dry mouth.

LOW ABUSE POTENTIAL AND RISK OF DEPENDENCE

SUNOSI is a schedule IV drug, and it has not shown evidence of tolerance, dependence, or withdrawal in clinical trials. The abuse potential was shown to be similar to or lower than that of the schedule IV stimulant phentermine, even at doses 8 times the maximum recommended daily dose.⁸

Advise patients that SUNOSI is a schedule IV drug, which is defined as a drug with low potential for abuse and low risk of dependence. Part of safety monitoring should include an evaluation for a history of drug abuse, particularly abuse with a stimulant or alcohol, and patients should be monitored for signs of misuse or abuse of SUNOSI.^{8,13}

BLOOD PRESSURE AND HEART RATE INCREASES

SUNOSI increases heart rate and systolic and diastolic blood pressure; these increases are dependent upon dose. Before initiating treatment with SUNOSI, blood pressure should be assessed and hypertension controlled.⁸

PRACTICAL CONSIDERATIONS

To support patient access to treatment, pharmacists can provide patients with information on available savings and coverage resources for SUNOSI. Greater than 90% of eligible commercially insured patients in the United States can get their prescription for as little as \$9 a month with the SUNOSI Savings Card.¹⁴ Advise eligible patients that they can review

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eligibility criteria and full terms and conditions, enroll, and download their SUNOSI® (solriamfetol) Savings Card at sunosihcp.com/savings-card-and-coverage.

For additional resources to use during counseling to help educate patients on their SUNOSI prescription, pharmacists can download patient education bro-

chures, a SUNOSI dosing card, and an ESS questionnaire at sunosihcp.com. Pharmacists can support screening for EDS by offering the downloadable ESS questionnaire to patients who visit the pharmacy with concerns of excessive sleepiness and refer them to a physician as needed for diagnostic assessment.

IMPORTANT SAFETY INFORMATION (CONT'D) DRUG INTERACTIONS

Do not administer SUNOSI concomitantly with MAOIs or within 14 days after discontinuing MAOI treatment. Concomitant use of MAOIs and noradrenergic drugs may increase the risk of a hypertensive reaction. Potential outcomes include death, stroke, myocardial infarction, aortic dissection, ophthalmological complications, eclampsia, pulmonary edema, and renal failure.

Concomitant use of SUNOSI with other drugs that increase blood pressure and/or heart rate has not been evaluated, and combinations should be used with caution.

Dopaminergic drugs that increase levels of dopamine or that bind directly to dopamine receptors might result in pharmacodynamic interactions with SUNOSI. Interactions with dopaminergic drugs have not been evaluated with SUNOSI. Use caution when concomitantly administering dopaminergic drugs with SUNOSI.

USE IN SPECIFIC POPULATIONS

Renal Impairment

Dosage adjustment is not required for patients with mild renal impairment (eGFR 60-89 mL/min/1.73 m²). Dosage adjustment is recommended for patients with moderate to severe renal impairment (eGFR 15-59 mL/min/1.73 m²). SUNOSI is not recommended for patients with end stage renal disease (eGFR <15 mL/min/1.73 m²).

ABUSE

SUNOSI contains solriamfetol, a Schedule IV controlled substance. Carefully evaluate patients for a recent history of drug abuse, especially those with a history of stimulant or alcohol abuse, and follow such patients closely, observing them for signs of misuse or abuse of SUNOSI (e.g., drug-seeking behavior).

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