Solriamfetol Titration and AdministRaTion (START) in Patients with Obstructive Sleep Apnea: A Retrospective Chart Review and Hypothetical Patient Scenario

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ABSTRACT

Introduction: Solriamfetol (Sunosi™), a dopamine/norepinephrine reuptake inhibitor, is approved (USA and EU) to treat excessive daytime sleepiness (EDS) in adults with obstructive sleep apnea (OSA) (37.5–150 mg/day). Real-world research on solriamfetol initiation is limited. The objective of this study was to describe dosing and titration strategies used when initiating solriamfetol and to assess whether and how patient factors affected these strategies.

Methods: This descriptive study, featuring a quantitative retrospective patient chart review and hypothetical patient scenario, enrolled US-based physicians prescribing solriamfetol for EDS associated with OSA and/or narcolepsy. Initiation of solriamfetol was classified as: (1) de novo (EDS medication-naive); (2) transition (switched/switching from existing EDS medication[s] to solriamfetol), or (3) add-on (adding solriamfetol to current EDS medication[s]). Study fielding occurred 3–19 June 2020. Data were summarized descriptively.

Results: Twenty-six physicians participated in the study, of whom 24 provided data from 50 patients with OSA (mean ± standard deviation [SD] age, 51.9 ± 9.1 years; 62% male). Mean apnea–hypopnea index at diagnosis indicated that most patients had severe OSA and 92% were adherent to positive airway pressure therapy. EDS was primarily moderate (56%) or severe (36%). Solriamfetol initiation was de novo for 44% of patients, transition for 52%, and add-on for 4%. Efficacy (including the need for better efficacy) was the primary reason for the initiation of solriamfetol as de novo (82%), transition (58%), and add-on (100%) therapy. Starting doses were predominantly 37.5 mg/day (48%) or 75 mg/day (48%); stable doses were typically 75 mg/day (56%) or 150 mg/day (40%). Most patients (64%) adjusted dosages once, reaching stable doses over a median (range) of 14 (1–74) days. Physicians considered EDS severity (32% of patients) when titrating,
but more commonly no specific patient factors caused them to alter their titration (44% of patients). Physicians abruptly discontinued wake-promoting agents (WPAs; 17/18, 94%) and stimulants (6/9, 67%) for transitioning patients. The hypothetical patient scenario showed that physicians discontinuing prior WPAs commonly considered the current dose (23%) and potential adverse events (15%). Most patients (96%) were stable on solriamfetol at data collection.

**Conclusions**: In a real-world study, most physicians initiated solriamfetol at 37.5 or 75 mg/day and titrated to 75 or 150 mg/day for patients with EDS associated with OSA, adjusted dosages once, and abruptly discontinued prior WPAs. At data collection, most patients remained on solriamfetol.
**Graphical abstract**

**Solriamfetol Titration & AdminisTraTion (START) in Patients With Obstructive Sleep Apnea: A Retrospective Chart Review and Hypothetical Patient Scenario**

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How do physicians prescribing solriamfetol for patients with excessive daytime sleepiness (EDS) in OSA formulate and execute initiation and titration strategies?

**Study Design**

- **26 US-based physicians** prescribing solriamfetol participated in a retrospective chart review and 24 provided data from 50 patients with OSA
- **Solriamfetol initiation strategies** were categorized as:
  - de novo – EDS medication-naive
  - transition – switched/switching from existing EDS medication(s) to solriamfetol
  - add-on – adding solriamfetol to current EDS medication(s)

**Results**

**Patients with OSA**

- **Solriamfetol initiation** was de novo for 44% (n=22), transition for 52% (n=26), and add-on for 4% (n=2) of patients
- **Efficacy** was the primary reason for starting solriamfetol, regardless of whether initiation was de novo (82%), transition (58%), or add-on (100%)

**Patients typically started solriamfetol at 37.5 or 75 mg/day and were stable at 75 or 150 mg/day**

- **Starting dose** distribution:
  - Overall: 44% 37.5 mg/day, 55% 75 mg/day, 8% 150 mg/day
  - De novo: 48% 37.5 mg/day, 41% 75 mg/day, 8% 150 mg/day
  - Transition: 54% 37.5 mg/day, 54% 75 mg/day, 5% 150 mg/day
  - Add-on: 46% 37.5 mg/day, 34% 75 mg/day, 1% 150 mg/day

- **Stable dose** distribution:
  - Overall: 50% 75 mg/day, 2% 150 mg/day
  - De novo: 58% 75 mg/day, 2% 150 mg/day
  - Transition: 73% 75 mg/day, 5% 150 mg/day
  - Add-on: 39% 75 mg/day, 5% 150 mg/day

**Key Takeaway**

- Most patients (84%) had 1 dose adjustment, and median time to a stable dose was 14 days. 96% of patients were on a stable dose of solriamfetol at data collection.
- Physicians abruptly discontinued wake-promoting agents (17/18, 94%) and stimulants (6/6, 67%) for transitioning patients.
In this study characterizing real-world dosing and titration strategies for solriamfetol in patients with obstructive sleep apnea, efficacy was the primary factor physicians considered for most patients when deciding to initiate solriamfetol.

Patients typically started solriamfetol at 37.5 mg/day (48%) or 75 mg/day (48%), required one dose adjustment (64%), and reached a stable dose of 75 mg/day (56%) or 150 mg/day (40%).

For patients transitioning to solriamfetol from prior medications, wake-promoting agents were almost always (17/18, 94%) discontinued abruptly.

Digitial Features

This article is published with digital features, including a graphical abstract, to facilitate understanding of the article. To view digital features for this article go to https://doi.org/10.6084/m9.figshare.20119322.

Introduction

Obstructive sleep apnea (OSA), a common breathing disorder affecting nearly 1 billion adults worldwide [1], is frequently associated with excessive daytime sleepiness (EDS) [2]. Continuous positive airway pressure (CPAP) is the primary therapy for OSA, although adherence varies [3], and persistent EDS is reported by 9–22% of CPAP-treated patients [4, 5]. Treatment of residual sleepiness in patients with OSA has been recommended by the American Academy of Sleep Medicine [6]. The wake-promoting agents (WPAs) modafinil and armodafinil have been the first-line pharmacologic treatments for residual EDS associated with OSA, but new options have recently been approved [7].

Solriamfetol (SunositM; Jazz Pharmaceuticals, Dublin, Ireland), a dopamine and norepinephrine reuptake inhibitor, demonstrated efficacy and safety in treating EDS associated with OSA in phase 3 clinical trials [8–10]. Solriamfetol was approved in 2019 in the USA [11] and 2020 in the EU [12] to treat adults with EDS associated with OSA (37.5–150 mg/day) or narcolepsy (75–150 mg/day). The recommended titration strategy for patients with OSA is to initiate treatment at 37.5 mg/day, after which the dose may be doubled at intervals of at least 3 days up to a maximum dose of 150 mg/day [11]. The most common treatment-emergent adverse events associated with solriamfetol treatment during clinical trials were headache, nausea, decreased appetite, nasopharyngitis, dry mouth, insomnia, and anxiety [8, 10, 13].

During clinical trials, patients used solriamfetol alone for EDS after washing out prior EDS medications [8, 9]. In clinical practice, however, patients may start solriamfetol while tapering other EDS treatments or add solriamfetol to their current regimen of EDS medications. There is no guidance in solriamfetol’s label specifically related to the initiation of solriamfetol when transitioning from or using alongside other EDS medications, nor is there guidance regarding tapering or discontinuation of other agents when switching to solriamfetol. Given the recent clinical availability of solriamfetol, data describing real-world physician dosing and titration strategies could help optimize patient care. Therefore, this study was designed to provide such evidence. Study objectives were to describe dosing and titration strategies used when initiating solriamfetol and to assess whether and how patient factors affected these strategies.
METHODS

Study Design

This virtual, descriptive study included a quantitative retrospective patient medical chart review and a cross-sectional qualitative survey of US-based physicians prescribing solriamfetol to patients with EDS associated with OSA (and/or narcolepsy; data from patients with narcolepsy reported separately). Study fielding occurred from June 3 to 19, 2020. The study was approved by a centralized independent review board (New England IRB 20201061) and was performed in accordance with the Declaration of Helsinki of 1964 and its later amendments. Informed consent was obtained from all individual participants included in the study.

Data Source and Participants

Eligible physicians were those who had prescribed solriamfetol to ≥ 3 patients with OSA (and/or narcolepsy) and were willing to include report information from three to five patient charts meeting the patient chart inclusion criteria of the study. Exclusion criteria included lack of access to a mobile device that could send and receive text messages (or lack of access to a computer) and being an employee or immediate family member of an employee of Jazz Pharmaceuticals. Medical charts were obtained from patients who met the criteria of age ≥ 18 years at screening, diagnosis of OSA, previously prescribed solriamfetol and reached a stable dose, and one of the following: (1) not taking any pharmacologic treatment for EDS when prescribed solriamfetol, (2) switched or were switching to solriamfetol from other EDS medication(s), or (3) adding solriamfetol to existing EDS medication(s) and intending to remain on both/all medications. Patients given solriamfetol during a clinical trial or early access program were excluded. Target enrollment was 25 physicians reporting information from three to five patient medical charts, for a total of 75–125 patient charts. Formal sample size calculations were not performed, given the descriptive nature of the study.

Procedures

Physicians who met the inclusion criteria were invited to participate. Physician eligibility was assessed through an electronic screener via text message or email, and consent was provided via an electronic informed consent form. Consenting physicians were provided detailed instructions on identifying and selecting patient charts that met the eligibility criteria. Participating physicians identified three to five eligible patient charts and entered all relevant information into a patient data collection form they accessed through their mobile device or computer.

Physicians were then asked to complete a qualitative survey by calling into an automated voice response system. Physicians had the option to grant or not grant permission to the study team to use their audio voice recordings for presentations, publications, and internal/external meetings. The automated voice response system asked open-ended questions pertaining to two scenarios: a hypothetical patient with OSA (Box 1) and a hypothetical patient with narcolepsy (reported separately). The hypothetical patient scenario helped to contextualize physician behaviors and decision-making related to real-world patients. All answers were recorded and transcribed.

Box 1. Hypothetical Patient Scenario
Imagine a physician colleague of yours came to you seeking advice about treatment for one of their patients named Joe. Joe is a 48-year-old male diagnosed with obstructive sleep apnea (OSA) who is currently being treated with modafinil and uses a continuous positive airway pressure (CPAP) machine for at least 6 h per night to control his excessive daytime sleepiness (EDS) symptoms. His current modafinil dose is 400 mg/day which he has been taking for 2 years. Joe has a body mass index of 35 (obese) and is currently taking a statin for hypercholesterolemia. While modafinil previously worked well to control his symptoms, he has developed a tolerance to the medication and it no longer works effectively to control his EDS. His most recent Epworth Sleepiness Scale rating was a 13. Your colleague would like to get your advice on starting Joe on solriamfetol.
Endpoints and Statistical Analysis

The following quantitative endpoints were assessed: (1) physician and patient characteristics; (2) treatment initiation strategies; (3) reasons for prescribing solriamfetol; (4) dosing strategies for solriamfetol and other EDS medications when titrating to solriamfetol; (5) factors physician considered when titrating; (6) use of other medications for EDS; (7) physician confidence in titration strategy, and (8) number of patients still on solriamfetol and reasons for discontinuation. Qualitative endpoints assessed for the hypothetical patient scenario were: (1) description of whether physician agrees or disagrees patient is appropriate for solriamfetol; (2) description of whether physician would add solriamfetol to patient’s current EDS treatment regimen or switch patient to solriamfetol (as well as titration approach physician would suggest, and factors physician would consider in choosing the approach); and (3) description of how the initial solriamfetol titration approach would change based on different patient factors (e.g., comorbidities, concomitant medications, lifestyle factors).

Analysis of physician characteristics included all enrolled physicians who recorded data on ≥ 1 patient chart. Analysis of patient characteristics was based on all recorded patient medical charts meeting the inclusion/exclusion criteria. Demographic and baseline characteristics were summarized descriptively. For continuous variables, the number (n), mean, standard deviation (SD), median, and minimum and maximum were described. For categorical variables, frequency counts and percentage of physicians/patients within each category were described. Missing or partially missing data were not imputed.

Data related to solriamfetol treatment were summarized overall and by solriamfetol initiation strategy. Solriamfetol initiation strategies were divided into 3 categories: de novo (patient not on any pharmacologic treatment for EDS when solriamfetol treatment was initiated), transition (patient switched or was switching to solriamfetol from ≥ 1 EDS medications), and add-on (patient added solriamfetol to ≥ 1 EDS medications already being taken and intended to remain on both/all medications). All quantitative data were analyzed using SAS version 9.4.

For the qualitative analysis from the hypothetical patient scenario, content analysis of the recordings identified themes in the responses, and a trained linguist captured language choice patterns based on discourse analysis techniques used in health care research [14]. Data for each endpoint were summarized descriptively.

RESULTS

Physician and Patient Characteristics

Of the 87 physicians recruited, 82 completed the screener, 29 met eligibility criteria, and 26 completed the study. All of the 26 physicians who completed the study responded to the hypothetical patient scenario, of whom 24 entered data from the charts of patients with OSA (Table 1). Physician specialties included internal medicine, neurology, pulmonology, psychiatry, and otolaryngology. Most were board-certified in sleep medicine. Mean time in practice (and in treating OSA) was ≥ 16 years. Physicians reported using solriamfetol in a combined total of 372 patients with OSA across the prior 12 months, with a mean (SD) of 14.3 (12.8) patients per physician.

Information was collected on 50 patients with OSA. Mean (SD) age was 51.9 (9.1) years, 62% were male, and most were overweight or obese (Table 2). EDS was primarily rated as moderate to severe when solriamfetol was first prescribed. Most patients were employed, either full- or part-time. Forty-three (86%) had comorbidities, of which the most common were obesity, cardiovascular disorders (most frequently hypertension), and type 2 diabetes. Most patients were using positive airway pressure therapy (CPAP, bilevel positive airway pressure, or automatic positive airway pressure) and were reported as adherent by their physicians at solriamfetol initiation (Table 3). The mean apnea–hypopnea index and mean respiratory disturbance index at time of OSA diagnosis indicated severe OSA.
Solriamfetol Initiation

Most patients (26/50; 52%) were transitioning to solriamfetol from other EDS medications (“transition” patients); 22/50 (44%) were initiating solriamfetol de novo (“de novo” patients); and 2/50 (4%) were adding solriamfetol to existing EDS medications (“add-on” patients).

Table 1 Physician characteristics

| Characteristic                        | All physicians (N = 26) | Physicians reporting data on initiating solriamfetol for patients with OSA (n = 24) |
|---------------------------------------|------------------------|----------------------------------------------------------------------------------|
| Specialty, n (%)                      |                        |                                                                                  |
| Internal medicine                     | 7 (27)                 | 6 (25)                                                                           |
| Neurology                             | 7 (27)                 | 7 (29)                                                                           |
| Pulmonology                           | 6 (23)                 | 5 (21)                                                                           |
| Psychiatry                            | 5 (19)                 | 5 (21)                                                                           |
| Otolaryngology                        | 1 (4)                  | 1 (4)                                                                            |
| Practice setting, n (%)               |                        |                                                                                  |
| Private practice                      | 21 (81)                | 20 (83)                                                                          |
| Regional/local/community hospital/clinic | 4 (15)                | 4 (17)                                                                          |
| Academic hospital                     | 1 (4)                  | 0 (0)                                                                            |
| Years in practice                     |                        |                                                                                  |
| Mean (SD)                             | 16.9 (6.8)             | 16.9 (7.0)                                                                       |
| Median (range)                        | 15.5 (5–29)            | 15 (5–29)                                                                        |
| Years treating patients with OSA      |                        |                                                                                  |
| Mean (SD)                             | 16.3 (6.5)             | 16.2 (6.8)                                                                       |
| Median (range)                        | 15.5 (2–26)            | 15.0 (2–26)                                                                      |
| Board-certified in sleep disorders (n, %) |                      |                                                                                  |
| Yes                                   | 19 (73)                | 17 (71)                                                                          |
| No                                    | 7 (27)                 | 7 (29)                                                                           |

OSA Obstructive sleep apnea, SD standard deviation

Table 2 Characteristics of study patients with obstructive sleep apnea

| Characteristic                        | Patients (N = 50) |
|---------------------------------------|-------------------|
| Age, years, mean (SD)                 | 51.9 (9.1)        |
| Sex, n (%)                            |                   |
| Male                                  | 31 (62)           |
| Female                                | 19 (38)           |
| Physician-reported EDS severity*, n (%)|                   |
| Mild                                  | 4 (8)             |
| Moderate                              | 28 (56)           |
| Severe                                | 18 (36)           |
| Current employment status, n (%)      |                   |
| Employed full-time (incl. self-employed) | 31 (62)           |
| Employed part-time (incl. self-employed) | 5 (10)           |
| Unemployed                            | 4 (8)             |
| Homemaker                             | 5 (10)            |
| Retired                               | 4 (8)             |
| Unknown                               | 1 (2)             |
| BMI, kg/m², mean (SD)                 | 32 (7.5)          |
| BMI category, n (%)                   |                   |
| Underweight (< 18.5 kg/m²)            | 0 (0)             |
| Normal (18.5–24.9 kg/m²)              | 5 (10)            |
| Overweight (25–29.9 kg/m²)            | 20 (40)           |
| Obese (≥ 30 kg/m²)                    | 25 (50)           |
| Comorbidities b, n (%)                |                   |
| Obesity                               | 25 (50)           |
| Cardiovascular disorders c            | 16 (32)           |
| Type 2 diabetes mellitus              | 14 (28)           |
| Psychiatric disorders d               | 7 (14)            |
| Fibromyalgia or chronic fatigue syndrome | 5 (10)           |
| Migraine headaches                    | 5 (10)            |
| Other sleep disorder                  | 4 (8)             |
Conversations about starting solriamfetol were primarily physician-initiated (48/50, 96%); 2/50 (4%) were patient-initiated. The most commonly cited primary reason prompting the discussion to prescribe solriamfetol de novo (82%) was its efficacy profile; a need for improved efficacy/augmenting the effects of other medications was the most common for patients transitioning to (58%) or adding on (100%) solriamfetol (Fig. 1).

When physicians were deciding to start the 43 patients with comorbidities on solriamfetol, they did not consider comorbidities as a factor in this decision for 31 (72%) of these patients. Among the other 12 patients with comorbidities, hypertension ($n = 9$), hyperlipidemia ($n = 6$), and arrhythmia ($n = 1$) were taken into consideration in the decision-making process.

Overall, most patients started solriamfetol at 37.5 mg ($n = 24/50; 48%$) or 75 mg ($n = 24/50; 48$%); 2/50 (4%) patients started at 150 mg, one of whom eventually titrated to 75 mg. Solriamfetol 75 mg was the most common starting dose among de novo patients, while 37.5 mg was more common among those transitioning; of those adding on, one patient each started at 37.5 mg and 75 mg. Across all patients, 75 mg was the most common stable dose ($n = 28/50; 56$%), followed by 150 mg ($n = 20/50; 40$%) and 112.5 mg ($n = 1/50; 2$%); one patient was erroneously listed at 125 mg. The most common

| Table 2 continued |
|-------------------|
| **Characteristic** | **Patients** |
| **(N = 50)**      |            |
| Other             | 4 (8)      |
| Renal impairment/disease | 2 (4) |
| None              | 7 (14)     |

*BMI Body mass index, EDS excessive daytime sleepiness
aPhysicians were asked to characterize overall severity of patients’ EDS at the time solriamfetol was prescribed, on a scale ranging from 0 (no EDS) to 3 (severe EDS)
bPatients could have > 1 comorbidity
Cardiovascular disorders included hypertension ($n = 9$), hyperlipidemia ($n = 6$), and arrhythmia ($n = 1$)
Psychiatric disorders included anxiety ($n = 4$), depression ($n = 2$), and attention deficit hyperactivity disorder ($n = 1$)

Table 3 Nonpharmacologic treatments, primary airway therapy adherence levels, and severity of obstructive sleep apnea (OSA) in patients with OSA

| **Variable** | **Patients** |
|--------------|--------------|
| **Nonpharmacologic OSA treatments when solriamfetol was initially prescribed, n (%)** |            |
| Lifestyle changes | 30 (60) |
| PAP therapya | 39 (78) |
| Oral appliances | 5 (10) |
| Surgery | 3 (6) |
| None | 3 (6) |
| Other | 1 (2) |

Adherence to PAP therapyab, n (%) ($n = 39$)

| Adherent | 36 (92) |
| Nonadherent | 2 (5) |
| Don’t know | 1 (3) |

Apnea–hypopnea index at OSA diagnosis ($n = 37$)

| Mean (SD) | 33.1 (19.7) |

Respiratory disturbance index at OSA diagnosis ($n = 16$)

| Mean (SD) | 41.0 (18.9) |

PAP Positive airway pressure
aIncludes continuous positive airway pressure, bilevel positive airway pressure, and automatic positive airway pressure
Physicians were asked to characterize patient adherence to PAP therapy as adherent or nonadherent, based on The Centers for Medicare and Medicaid Services (CMS) definition of adherence (i.e., using the device for ≥ 4 h per night for 70% of nights [21 nights] during a consecutive 30-day period)
stable dose for de novo and add-on patients was 75 mg, while 150 mg was most common among those transitioning (Fig. 2a). Most patients (n = 32/50; 64%) had one dose adjustment to reach their stable dose, though de novo and add-on patients typically had fewer dose adjustments than those transitioning to solriamfetol (Fig. 2b).

For those requiring dose adjustments (n = 39), median (range) time to reach a stable dose was 14 (1–74) days. Median (range) times for de novo (n = 14) and transitioning (n = 24) patients were 18 (3–45) days and 14 (1–74) days, respectively. One patient with add-on treatment required a dose adjustment and reached a stable dose in 7 days. Most patients (n = 48/50, 96%) were still on a stable dose of solriamfetol at data collection. Two patients discontinued solriamfetol, one because of lack of efficacy and one because of increased blood pressure.

When deciding how to titrate solriamfetol, physicians reported they did not consider any specific patient factors for 22/50 (44%) patients. Among factors considered, the most common were EDS severity (32% of patients) and patient comorbidities (20% of patients) (Fig. 3). Hypertension (n = 5), anxiety and obesity (n = 2 each), and type 2 diabetes, migraines, and liver disease (n = 1 each) were the comorbidities that most influenced titration decisions.

**Prior EDS Medications**

In total, 28 patients were taking EDS medication(s) prior to solriamfetol initiation (i.e., 2 add-on and 26 transitioning). Both add-on patients were taking methylphenidate alone; one had their methylphenidate dose adjusted at solriamfetol initiation. Of the transitioning patients, 24 were on one previous EDS medication, and two were on two previous EDS medications; 18 had been taking WPAs, and ten had been taking a stimulant (9 of the 10 were transitioned off the stimulant; one patient who had been on both a stimulant and a WPA remained on the stimulant but switched off the WPA). Of the patients transitioning from a WPA (n = 18), 17 (94%) discontinued abruptly, and one tapered off while starting solriamfetol (Fig. 4). The patient tapering off a WPA did so over three dose adjustments (which occurred before starting solriamfetol). Of those transitioning from a stimulant (n = 9), six discontinued abruptly, and three tapered off while starting solriamfetol (Fig. 4). Of the three patients tapering off stimulants, two had two dose adjustments of the stimulant before starting solriamfetol, and one had none; after starting solriamfetol, two
patients had one stimulant dose adjustment, and one had two adjustments.

For each medical chart, physicians were asked to rate how likely they were to recommend their approach to a colleague with a similar patient. Physicians were likely or very likely to recommend the approach used for 100% of de novo and add-on patients and 88% of transitioning patients (physicians were neutral towards recommending the approach used for the other 12% of transitioning patients).

**Hypothetical Patient Scenario**

All 26 physicians thought solriamfetol was appropriate for the hypothetical patient (Box 1). Most physicians (65%) cited this patient’s lack of symptom control with modafinil as a reason for solriamfetol treatment being suitable; a high modafinil dose (31%) and severity of EDS (27%) were also commonly cited. Most physicians (81%) recommended transitioning to solriamfetol, while 15% suggested adding solriamfetol to the modafinil treatment, and 4% said it depended on other (unspecified) factors. When asked how they would titrate

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**Fig. 2** Dosing strategies. a Starting and stable solriamfetol doses. Because of a data input error, data on the final dose for 1 participant (4%) in the transition group are missing. b Number of dose adjustments to reach a stable dose of solriamfetol. Due to rounding, values do not add to 100%
solriamfetol, 46% reported they would follow the label; the other 54% suggested an alternative approach. Most physicians with an alternative approach (12/14, 86%) would start at 75 mg instead of 37.5 mg; one physician would start at 37.5 mg and titrate to 75 mg, then 112.5 mg, and finally 150 mg; and one would start at a “low dose” (not further specified). Some physicians expressed that the 37.5 mg dose would not be effective due to the patient’s symptom severity. Among physicians who indicated a final dose or dose they would aim for (n = 23), one indicated a 75-mg final dose, 15 would aim for 75 mg and progress to 150 mg if 75 mg was insufficient, and seven would aim for 150 mg.

Regarding how physicians would discontinue modafinil, the most commonly suggested strategy was abrupt discontinuation (39%), followed by several tapering strategies (taper

**Fig. 3** Factors taken into consideration by physicians when titrating to solriamfetol. *EDS* Excessive daytime sleepiness

**Fig. 4** Discontinuation approach for other EDS medications among patients who transitioned to solriamfetol. *EDS* excessive daytime sleepiness
modafinil and assess the need to discontinue while starting solriamfetol [19%]; taper and discontinue before starting solriamfetol [19%]; and taper and discontinue while starting solriamfetol [15%]); as well as other approaches (8%). Factors physicians cited as influencing their titration approach for modafinil included current modafinil dose (23%), likelihood of adverse reaction (15%), similar mechanism of action (12%), EDS severity (4%), and other (unspecified) factors (12%) (> 1 factor could be cited); 42% of responding physicians stated no factors had influenced their titration approach. When physicians were asked for their titration approach if the patient was not taking modafinil, 42% responded they would follow the label; the other 58% responded they would take an alternative approach (for 93% of them, start at 75 mg). As to whether the presence of hypertension controlled with antihypertensive medication would affect their approach, most physicians (81%) suggested it would not, indicating they could easily track any issues by monitoring blood pressure.

**DISCUSSION**

This study reported real-world dosing and titration strategies from 26 experienced physicians across five medical specialties. Most patients were transitioning to solriamfetol from prior EDS medications. The majority of patients were considered to have moderate or severe EDS by their clinicians prior to starting solriamfetol, which was the factor most often considered by clinicians when deciding on their titration approach, including starting dose. Solriamfetol was primarily initiated at 37.5 or 75 mg. Patients usually required at least one dose adjustment before reaching their stable dose of solriamfetol, which was typically 75 mg or 150 mg; no patients were stable at the 37.5 mg dose. Physicians were overall confident in their treatment approaches, and only two patients discontinued solriamfetol before data collection. Responses to the hypothetical patient scenario included titration strategies and rationales consistent with those used for the physicians’ patients.

Titration strategies that maximize efficacy while allowing physicians to gauge patient response and minimize safety risks are critical for optimal treatment [15]. The participating physicians sometimes initiated solriamfetol above the dose recommended by the label, at 75 mg or 150 mg, but the median 14 days to reach a stable dose (across all groups) indicated that physicians generally titrated at intervals longer than the 3 days the label suggests as the minimum interval. In response to the hypothetical patient scenario, one physician stated the preference to allow patients to remain on a dose for 3–4 weeks and re-adjust at the next clinic visit. Such an approach may explain the long titration time reported for some patients. Most patients had one adjustment to reach their stable dose, but the number varied across the groups, and de novo patients were more likely to be stable on their initial dose level than were patients transitioning to solriamfetol from another EDS medication. While most patients taking either WPAs or stimulants had their prior EDS medication abruptly discontinued, patients taking stimulants were overall more likely to be tapered off their medication. Differences in discontinuation strategies may be related to known issues of rebound hypersomnolence and withdrawal symptoms associated with stimulant discontinuation [16]. In combination with the titration strategy selected by physicians when initiating solriamfetol, these approaches may help to properly assess efficacy and minimize side effects in patients. Evidence on the selection of these strategies is particularly important given that solriamfetol’s label contains no guidance on how to transition to solriamfetol from other EDS medications. A large majority of physicians were satisfied with their approach to transitioning patients to solriamfetol, suggesting that physicians deemed their approach to be successful in most cases.

Although most patients had comorbidities representative of those seen in general populations of adults with OSA [17], physicians were more likely to consider EDS severity than comorbidities when deciding on titration strategies for solriamfetol. Of the nine patients with comorbid hypertension, five had it...
considered by their physician when starting solriamfetol, making it the most frequently considered comorbidity. This strategy aligns with the solriamfetol label’s guidance to monitor blood pressure before and during solriamfetol treatment and with the dose-related small mean increases in blood pressure observed in the clinical trial of solriamfetol for patients with EDS associated with OSA [8]. When asked how controlled hypertension would affect their treatment strategy for a hypothetical patient, most physicians indicated there would be no impact, given the ability to monitor blood pressure.

Core strengths of this study were the participation of highly experienced physicians from diverse specialties and the similarities between the patient cohort and larger, real-world populations of patients with OSA [17]. Nevertheless, the study had several limitations. The study utilized feedback from physicians in the USA, where other medications for EDS are currently on the market. Clinician experiences outside the USA may differ, considering the dearth of medications approved to treat EDS in OSA, it is less likely that patients would be taking other EDS medication when starting solriamfetol. The impact of solriamfetol initiation and titration strategies on side effects, EDS symptom severity, and CPAP adherence during titration were not assessed. Only two patients were adding solriamfetol to existing treatments, limiting the generalizability of findings from this group. Data for these patients were included for completeness, as the add-on strategy was part of the study design; however, no conclusions can be drawn based on these two patients. Finally, physicians were asked to characterize overall EDS severity using a 0 (no EDS) to 3 (severe EDS) scale. This scale was chosen, rather than a standard scale such as the Epworth Sleepiness Scale, due to lack of consistent utilization of such scales in clinical practice; however, this nonstandard reporting may limit the ability to compare the EDS severity of this population with other study populations in the published literature.

CONCLUSION

In conclusion, efficacy, including the need for improved efficacy, was a key consideration for physicians prescribing solriamfetol in a real-world sample of patients with OSA, whether treatment was de novo, transition, or add-on. Physicians predominantly started solriamfetol at 37.5 mg or 75 mg, abruptly discontinued prior WPAs, and made one adjustment to reach a stable dose (typically 75 or 150 mg/day) over a median of 14 days. Most patients were still on a stable dose of solriamfetol at data collection, and physicians were confident in recommending the treatment approach they used with most patients described.

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**Data Availability.** All relevant data are provided within the manuscript and supporting files.

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