Clinician Directions for Use

Somryst™ Prescription Digital Therapeutic

Get Started

Rx Only
Caution: Federal Law restricts this device to sale by or on the order of a licensed healthcare professional in accordance with the law of the state in which that person practices to use or order the use of the device.

Legal Manufacturer: Pear Therapeutics Inc., 201 Mission St. #1450, San Francisco, CA 94150
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Somryst™, a mobile app is a 9-week Prescription Digital Therapeutic (PDT) for chronic insomnia.

Somryst Product Overview

Somryst is a 9-week Prescription Digital Therapeutic (PDT) for chronic insomnia. Somryst can be used on a mobile device, such as a smartphone or tablet. Somryst is available by prescription only. A licensed Health Care Provider (HCP) must prescribe Somryst and use of Somryst™ should be undertaken only under the supervised care of a Health Care Provider.

Somryst delivers digital Cognitive Behavioral Therapy for Insomnia (CBT-I) therapeutic content. CBT-I is a neurobehavioral treatment that focuses on addressing the maladaptive behaviors, routines, and dysfunctional thoughts that perpetuate sleep problems, regardless of the original source of the sleep problem.
CBT-I is typically delivered by a specialty-trained clinician, either 1:1 or in group format. Standard delivery of CBT-I usually occurs in weekly sessions over 6-8 weeks. CBT-I can be conceptualized as six sessions or Cores that deliver proven behavioral and cognitive treatment strategies. Somryst™ delivers treatment with the following 6 treatment Cores:

1. **Get Ready:** This Core sets the stage for the therapeutic experience. It lets patients know what they will need to learn and do to improve sleep.

2. **Sleep Window:** This Core is one of the most important ones. The patient will receive their first Sleep Window — a recommended Bedtime and Arising Time.

3. **Behaviors:** This Core helps patients identify and change certain habits and behaviors that can interfere with sleep. It establishes the key guidelines of CBT for insomnia

4. **Thoughts:** This Core explains how a patient’s thinking can contribute to insomnia. The patient will learn to identify and shift problematic thought patterns.

5. **Education:** This Core helps patients figure out what changes in their lifestyle and environment can promote better sleep.

6. **Looking Ahead:** This Core pulls together what patients have learned, prepares patients for the future, and teaches them what to do if they experience a relapse.

The Cores typically follow this structure:

- **Review:** Review of the previous week’s sleep (after the first Core, “Get Ready”), as collected in a sleep diary, and of homework (practiced strategies) from the previous week

- **Session Objectives:** Provides the rationale for the new treatment Core

- **Main Content:** Introduces new treatment content and strategies

- **Summary:** Wraps up the session by recapping above

- **Assignment:** Assignment of homework/strategies for upcoming week

Somryst includes a daily Sleep Diary in which patients record information about their sleep. The My Stuff section provides selected resources and elements from each Core for review. The My Stuff section for each Core is available after the Core is completed.
**Indications for Use**

Somryst™ is a prescription-only digital therapeutic intended to provide a neurobehavioral intervention (Cognitive Behavioral Therapy for Insomnia (CBT-I)) to patients 22 years of age and older with chronic insomnia.

Somryst treats patients with chronic insomnia by improving a patient’s insomnia symptoms.

**Who Should Use Somryst**

Your patient should only use Somryst if they:

- Are 22 or older with chronic insomnia
- Are able to read and understand English
- Have regular access to a mobile device (such as smartphone or tablet)
- Are familiar with how to use mobile apps (applications)
- Are able to upload data periodically, i.e., have internet/wireless connection access
- Are under the supervision of a Health Care Provider

**Who Should Not Use Somryst**

(Contraindications)

Somryst uses sleep restriction and consolidation, limiting the time a patient spends in bed to match the amount of time they sleep. This treatment technique can increase risks to some patients whose pathophysiology may be worsened. Because of this, it is not appropriate for everyone.

Patients with the following conditions or disorders should not use Somryst:

- Any disorder exacerbated by sleep restriction (e.g. bipolar disorder, schizophrenia, other psychotic spectrum disorders)
- Untreated obstructive sleep apnea
- Parasomnias
- Epilepsy
- Individuals at high risk of falls
- Individuals who are pregnant
- Individuals who have any other unstable or degenerative illness judged to be worsened by sleep restriction delivered as part of CBT-I
The Benefits of Somryst™

Use of Somryst can result in significant and lasting improvements to insomnia symptoms for your patients. Results from the Somryst Pivotal Studies showed patients experience a significant reduction in severity of insomnia after treatment, with more than 40% of the patient group no longer meeting the criteria for insomnia.

Therapeutic benefits from the use of Somryst are only possible for your patients if they follow the instructions and practice the exercises and strategies provided in the program. Treatment results may vary for your patients.

Risks associated with using Somryst are described in the “Safety Information and Warnings” section on next page.
Safety Information and Warnings

Somryst™ is not for everyone. Please use your clinical judgment to determine whether Somryst is right for your patient.

- Somryst is not for emergency use. Please instruct patients to dial 911 or go to the nearest emergency room in the event of a medical emergency.
- Patients should be clearly instructed not to use Somryst to communicate severe, critical, or urgent information to their Health Care Provider.
- Somryst is meant to be used as treatment with supervision of a Health Care Provider.
- Somryst is not meant to be a substitute for any treatment medication.
- Somryst contains sensitive medical information. Please instruct patients to protect their information by password-protecting their smartphone or tablet, and ensuring no one else may access their device.
- Sleep Restriction (and Consolidation) within Somryst can cause sleepiness, especially in the early stages of using the PDT. Somryst should not be used if the patient needs to be alert or cautious to avoid serious accidents in their job or daily life. Examples include:
  - Long-haul truck drivers
  - Long-distance bus drivers
  - Air traffic controllers
  - Operators of heavy machinery
  - Some assembly line jobs

- The usage data collected in therapy lessons by Somryst are not intended to be used as a standalone assessment of treatment progress.

Note: In the early stages of treatment, increased daytime sleepiness may be expected, but is usually temporary. Please instruct the patient to consult with their HCP if these experiences do not go away over a few weeks, as it may indicate that they have another sleep disorder or medical condition other than insomnia. Please instruct the patient that if they have trouble staying awake while performing potentially dangerous tasks (like driving) at any point in the treatment, to avoid these dangerous tasks or stop following the sleep restriction component of the therapy.

Please instruct the patient to read and follow the instructions provided in each module, and to stay with the therapy until the end to achieve the best results with Somryst. Please instruct the patient that it is important to give honest and accurate answers when reporting sleep results.
Somryst™ Product Description

Downloading Somryst

Your patients will have to download Somryst to access the product. Below are instructions needed to obtain access to Somryst:

To download Somryst on the iPhone or iPad:

- Tap the App Store icon on the home screen
- Tap the search icon and type “Somryst”
- Tap the “Get” button. The patient may need to enter their Apple ID and Password, or use Touch ID or Face ID to approve the download
- When Somryst is downloading, the Somryst icon will be visible on the home screen. Download progress is indicated within the icon
- Tap the Somryst icon to open the app when download completes

To download Somryst on an Android phone or tablet:

- Tap on the Play Store app on the Android phone
- Tap on the search bar and type “Somryst”
- Tap “Install”
- When Somryst is downloaded, either tap “Open” in the Play Store or, go to the home screen and tap the Somryst icon

Compatible Devices

Somryst is compatible with smartphone and tablet devices running:

- iOS version 11 or higher
- Android version 7 or higher

Please ensure your patient’s smartphone or tablet is running an Operating System (OS) version matching those above. If not, then please instruct the patient to update their software version before downloading and using Somryst.
The Patient Therapeutic Mobile Application

Getting Started

When Somryst™ is prescribed, the patient will receive an Access Code to activate the Somryst prescription. The patient must launch the Somryst therapeutic software application. During the initial onboarding, the patient’s device must be connected to the Internet. The patient must enter the access code and his or her email address. This step will verify and activate the prescription.

After the access code and email are verified, the patient will be asked to set up a password. Passwords must be at least 8 characters long, include one capital letter, and one special character.

The following special characters are accepted: ! @ # $ % ^ & * ( ) + = ” ? / > <

Next, re-enter the password.

SET A PIN

After setting a password, the patient will need to set up a 4-digit Personal Identification Number (PIN) for Somryst. This will secure the app when they are not using it. Setting a PIN will allow patients to quickly re-authorize access to Somryst by entering their 4-digit PIN, using their fingerprint, or using their face to unlock the app.

The patient can then log in and get started using Somryst. Somryst will show the log-in screen. The email and newly-created password can be used to log in.
**Getting Around**

This section describes how to navigate between the different areas of Somryst™.

**Basic Navigation**

Instruct the patient to use the tab bar at the bottom of the screen to move between the main sections of Somryst. The active section will be highlighted.

The arrows at the bottom of the screen lets the patient turn pages to read through the Core lessons. They can move forward or backward when the arrow is shown on the right or left side of the screen.

Access Help from the top of the home screen. The Help section contains information about how to use Somryst, including these directions.
Using the Tab Bar

The tab bar allows the patient to move easily between different sections of Somryst.

- **Home**
  - Tapping the **Home icon** takes the patient to the home screen. Tap this icon from anywhere in Somryst to go home.

- **Cores**
  - The **Cores icon** takes the patient to the list of Core modules. If a Core is available, it will be listed in blue. Unavailable Cores are shown in gray text with a lock icon.

- **Insights**
  - The **Insights icon** takes the patient to the Sleep Diary and Wake charts. This section also contains other useful information from their Sleep Diaries.

- **My Stuff**
  - Tap the **My Stuff icon** to review important information from each Core.
**Somryst™ Features**

The most important sections of Somryst are described in the following pages.

**Home**

On the Home screen, patients will find important information about their progress in the program and what they should do next. When a Sleep Window is available, patients can see their assigned bedtime and arising time. The number of sleep diaries entered for the week is also shown. Patients can also read an explanation of this week’s Core.

**Sleep Diaries**

By entering Sleep Diaries, the patient collects important information about their sleep patterns, and track their progress in the program. To provide Somryst the most accurate information, patients complete the Sleep Diary every day. If possible, the Sleep Diary should be completed within one hour of getting out of bed. Patients can enter Sleep Diaries for the current day and the previous two days. The Sleep Diary can always be accessed from the home screen.

The Sleep Diary can be used to track sleep for people who are awake or asleep at unusual times. In the Sleep Diary, the word “day" refers to the time when your patient is awake. The term “bed" refers to when your patient usually sleeps. Patients should not worry about giving exact times, and should not watch the clock. Patients should just give their best estimate when completing the Sleep Diary.
**Cores**

The Cores screen shows the 6 Cores of Somryst.

Cores provide new treatment techniques. When Cores are available, patients will see a button that, when tapped, will begin the Core. Tapping the 🔄 icon will show a list of the topics in each Core. Cores that are not yet available show a gray lock icon.

If patients leave the Core, they can pick up again where they left off. Cores that patients need more time to complete show a progress bar at the top.

**Insights**

The Sleep and Wake Charts show your patients sleep pattern for the previous seven days. The patient can also view important information from their Sleep Diary, such as the quality of your sleep and any sleep medicines logged for the week.

Patients can use the arrows at the top of the screen to show data for previous weeks.
**My Stuff**

My Stuff allows the patient to easily review important information from Cores they have already finished. The patient can always revisit this information from within the Core, but My Stuff provides a shortcut.

Each Core’s My Stuff information is unlocked after patients have completed that Core.

**Notifications**

Somryst™ will send patients notifications to help keep them on track. They will receive reminders to log their daily Sleep Diary, as well as notifications when new Cores are available.

Notifications help patients stay on track and make progress in sleep therapy.
Mobile Application Support

**Security**

Please remind patients that it is their responsibility to secure their mobile device (smartphone or tablet). If the patient uses an iPhone or iPad, they should use a 6-digit passcode known only to them. If available, Touch ID or Face ID should be used. If the patient uses an Android phone or tablet, they should use a password or 6-digit passcode and enable fingerprint-unlock if available.

It is the patient’s responsibility to update their phone or tablet operating system when recommended by the platform vendor (Apple or Google). Important security updates are included in operating system upgrades. The vendor will do this by notifying the patient on their device that an update is available for download and install.

**Replacing A Device**

If the patient needs to replace their smartphone or tablet, they should download Somryst™ again from the Apple Appstore or Google Play store and log in with their email address and password. The patient’s progress in the program is saved with the Somryst™ prescription, so the patient will be returned to the place where he or she left off.

**Updating Somryst**

If an update is available for Somryst, an alert will appear when the patient next opens Somryst. To update:

- Tap “Yes” to confirm that you would like to install the update
- Somryst will close, and patients will see the home screen of their smartphone or tablet.
- The Somryst icon will display the download progress
- When the update is complete, a colored dot will appear next to the Somryst name. This indicates a new version has been downloaded.
- Tap the icon to open Somryst.
**Updating Somryst™ (continued)**

For instructions on how to set up automatic app updates on a phone or smart device, visit the following web pages:

- [Apple Support](#)
- [Google Play Support](#)

For instructions on how to update the operating system (iOS or Android) of the phone or smart device, visit the following web pages:

- [iOS Updates](#)
- [Android Updates](#)

**Traveling with Somryst**

When traveling, the patient should follow the instructions below to ensure use of Somryst:

- Date and Time settings should be automatic. When connecting to a new network, the phone or smart device updates the time zone.
- If the time zone does not automatically adjust, go to the date and time settings to find the correct time zone, or to set the time zone back to automatic.
- Turning off cellular data will allow Somryst to be used without a network. A Wi-fi connection is required to play video and update the server with new data, including Sleep Diaries and Sleep Window. The patient must ensure that the mobile device is at least connected to available Wi-fi when traveling.
- Somryst cannot be updated unless the mobile device (smartphone or tablet) is connected to Internet (e.g., cellular data or Wi-Fi).

**Additional Support**

For additional support the patient can contact their Health Care Provider, or contact Somryst support at:

**Email:** pearconnect@peartherapeutics.com.

**Phone:** (833) 697-3738
Somryst™ Prescriptions

Dose and Frequency
Patients should be clearly instructed to complete a dose of all 6 treatment Cores. Patients who have completed all 6 Cores have shown the best outcomes.

Each core should be completed on a frequency of one core every 7 days.

Patients should complete their Sleep Diary daily and follow the sleep restriction window recommendations provided by Somryst.

Duration and Extension
Patient access to Somryst will automatically discontinue after 9 weeks (63 days). The prescription will end automatically based on the start date. Additional 9-week use of the therapy may benefit the patient, as insomnia is a chronic disease.
Clinician Dashboard

Accounts

After prescribing and enrolling your first Somryst™ patient, you will receive a message to the email address that you provided. The onboarding email contains a link that, when clicked, allows you to verify your account and set a password.

You can log into the Somryst Clinician Dashboard by visiting www.pear.md. Consider bookmarking this website for easy subsequent access. After navigating to this page, type in your email address and password and click the “Login” button. If you forget your password, click the “Forgot password?” link, enter your email address and click the “Send” button. An email will be sent to your email address with a link to set a new password.
The Patient Summary

Immediately after logging in, a summary view will be displayed. The summary view contains information for each patient:

- First and last name
- Date of birth
- Product
- Health Care Provider name
- Prescription start date
- Prescription days remaining

An example of the patient summary table can be viewed in the screen below:

You can log out of the Clinician Dashboard by clicking on the menu in the upper right and selecting “Log Out.” If you are signed in but are no longer interacting with the system, the website will automatically log you out after 15 minutes.

Clicking on a row in the Patient Summary displays the Somryst™ Dashboard for the selected patient.
Viewing Patient Data

Within the Clinician Dashboard, clinicians are able to view patient progress and patient clinical information (e.g., insomnia severity, sleep diary-derived variables, including wake after sleep onset, sleep onset latency). At the top of the dashboard, a prescription selector is displayed. The default is the current prescription. If applicable, you may select a previous prescription and view the relevant patient information gathered during that previous prescription.

A brief patient overview is displayed showing name, date of birth, prescription length and start date, and the Somryst™ product name.
Viewing Patient Data (continued)

Below the patient overview, patient sleep and assessment data are displayed. For each Core in the 9-week treatment, you can view the Sleep Efficiency percentage and Insomnia Severity Index (ISI). For alternating Cores, you can view the Patient Health Questionnaire 8 (PHQ-8) scores, which inquire about symptoms over the previous 2 weeks. A data table with detailed information for each treatment week can be viewed.

Noting whether a patient is using the program or failing to progress can be an important discussion point in the HCP encounter. HCPs may want to problem-solve barriers to use or may want to consider a different treatment if multiple attempts to engage fail. If the patient is not progressing clinically, the HCP may also want to decide whether to augment the treatment, extend the prescription, or consider a new treatment. The Clinician Dashboard allows HCPs to stay in sync with their patients, and better understand their patient’s journey between visits.
Clinical Studies

The therapeutic content in Somryst™ was evaluated in two randomized clinical trials to demonstrate safety and effectiveness.

The GoodNight Study

Therapeutic content delivered in Somryst™ was validated in multiple randomized clinical trials. This data set includes “The Good Night Study,” a large randomized controlled trial sponsored by the National Health and Medical Research Council (NHMRC) of Australia (ACTRN12611000121965)\(^1\,2\,3\). The Somryst PDT was tested as equivalent clinical content, under the name Sleep Healthy Using the Internet (SHUTi), which was accessed via a browser\(^1\,2\). Somryst delivers equivalent Therapeutic content via a native mobile software application.

The study was designed after prior clinical trials to further evaluate, among other things, Somryst in a population of patients with chronic insomnia.

Study participants (n=1149) were between the ages of 18-64, with symptoms of depression (PHQ-9 score between 4 and 20), with insomnia symptoms as documented by a score of 3 or above on at least one of the first four items of the Bergen Insomnia Scale (BIS) and score of 3 or above on at least one of the last 2 items and met criteria for chronic insomnia per Modified Morin’s Insomnia Interview. Participants with Major Depressive Disorder were excluded from this study.

All study participants received usual care (UC) consisting of behavioral treatment, pharmacotherapy and/or self-treatment (e.g., visit to a general practitioner for sleep and/or mood problems, pharmacotherapy (e.g., for sleep and/or mood problems), over-the-counter sleep aids, visit to a sleep specialist, visit to a mental health provider).

Participants were randomized 1:1 to 9 weeks of treatment with the following:

- UC+SHUTi: Usual Care + SHUTi (now known as Somryst)
- UC+Control: Usual Care + Attention-matched, Digital Control
The GoodNight Study (Continued)

The Digital Control intervention (HealthWatch) was an interactive health and lifestyle web program that contained information about a range of health content (e.g., environmental health, nutrition, activity, medication) but had no specific mental health or sleep-related content. HealthWatch also administered weekly surveys on these topics to match for interaction required in the treatment group.

Participants in the UC+SHUTi group (n=574) were asked to complete all six Cores within the 9-week treatment period. Participants randomized to UC+Control (n=575) were asked to complete nine internet-delivered modules within the 9-week treatment program, thus matching the attention components of SHUTi. Insomnia symptoms were evaluated for all participants at baseline, the end of the 9-week treatment period and the 6-month, 12-month, and 18-month follow-up via the Insomnia Severity Index (ISI) and sleep diaries. Sleep diaries were administered online and collected for a period of 10 days (within a 2-week window), at each assessment time point. Sleep diaries were used to calculate diary-derived composite variables, including sleep onset latency (SOL, minutes to fall asleep) and wake after sleep onset (WASO, minutes awake during the night).
The GoodNight Study (Continued)

**Endpoint Analysis: Insomnia Severity and Symptomatology**

Insomnia severity was assessed using the ISI. ISI scores were analyzed using a mixed model repeated measures ANOVA with factors for treatment, time, and treatment time interaction. Least-Squares (LS) mean ISI scores for each treatment group were compared at baseline, at the end of the treatment (week 9), and at month 6, and month 12 follow-up. The analysis included all available data for participants randomized in the trial.

**Table 1.** Effect of therapy on insomnia symptoms (ISI) by assessment timepoint.

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>UC+SHUTi</th>
<th>UC+Control</th>
<th>LS Mean Differences (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of Subjects</td>
<td>LS Mean</td>
<td>Number of Subjects</td>
<td>LS Mean</td>
</tr>
<tr>
<td>Baseline</td>
<td>574</td>
<td>15.92</td>
<td>575</td>
<td>16.23</td>
</tr>
<tr>
<td>End of Treatment Period (Week 9)</td>
<td>250</td>
<td>7.23</td>
<td>342</td>
<td>13.18</td>
</tr>
<tr>
<td>Month 6 Follow-up</td>
<td>226</td>
<td>7.65</td>
<td>280</td>
<td>12.13</td>
</tr>
<tr>
<td>Month 12 Follow-up</td>
<td>162</td>
<td>7.62</td>
<td>230</td>
<td>11.40</td>
</tr>
</tbody>
</table>

Note: p values are not adjusted for multiplicity and analyses are based on available patient data.

A comparison of LS mean ISI scores is shown in Table 1. Insomnia severity symptoms were comparable across treatment groups at baseline (p=0.2120). LS mean ISI scores were in the clinical insomnia range (score > 15). Insomnia severity symptoms were reduced at week 9 (p<0.0001), month 6 (p<0.0001), and month 12 (p<0.0001) follow-up among participants who received UC+SHUTi as compared to UC+Control.
The GoodNight Study (Continued)

To evaluate the change in insomnia severity symptoms over baseline, the change in ISI score from baseline to week 9, month 6, and month 12 follow-up were analyzed for each treatment group (Table 2). The average reduction in ISI score was greater at week 9, month 6, and month 12 for the UC+SHUTi group (mean -8.63, -8.17, and -8.21, respectively) than the UC+Control group (mean -2.85, -3.86, and -4.63). The difference between groups was significant at each timepoint (p<0.0001).

Table 2. Effect of therapy on change from baseline (ISI) by assessment timepoint.

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>UC+SHUTi</th>
<th>UC+Control</th>
<th>LS Mean Differences (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>End of Treatment Period (Week 9)</td>
<td>250</td>
<td>-8.63</td>
<td>342</td>
<td>-2.85</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-5.78 (-6.50, -5.06)</td>
</tr>
<tr>
<td>Month 6 Follow-up</td>
<td>226</td>
<td>-8.17</td>
<td>280</td>
<td>-3.86</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-4.31 (-5.09, -3.53)</td>
</tr>
<tr>
<td>Month 12 Follow-up</td>
<td>162</td>
<td>-8.21</td>
<td>230</td>
<td>-4.63</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-3.59 (-4.46, -2.71)</td>
</tr>
</tbody>
</table>

Note: p values are not adjusted for multiplicity and analyses are based on available patient data.

Improved insomnia symptom severity was observed in the intent-to-treat study population, demonstrating efficacy of UC+SHUTi in reducing chronic insomnia symptoms. Participants who received UC+SHUTi showed statistically significant improvement in overall insomnia symptom scores, as well as the within group change in insomnia symptom scores, over UC+Control. Insomnia symptom severity was improved at the end of the treatment period and this effect was maintained to month 12 for the participants randomized to UC+SHUTi.

Participants randomized to UC+SHUTi demonstrated more than a 7-point reduction in insomnia symptom score on average, representing a clinically significant change in insomnia severity. Furthermore, by the end of the treatment period participants receiving SHUTi no longer met the threshold for clinical insomnia. This effect of treatment was maintained up to the month 12 follow-up. In contrast, participants receiving UC+Control maintained a symptom severity status registering above “no clinically significant” insomnia, on average, at the end of the treatment period and at the month 6 follow-up.
The GoodNight Study (Continued)

*Additional Insomnia Analysis: Insomnia Severity Symptoms During Intervention (Weeks 2, 4, 6, and 8)*

An analysis of insomnia severity symptoms measured every other week during the treatment period was performed. The LS mean ISI scores for the UC+SHUTI and UC+Control groups are shown for each timepoint during the intervention period in Table 3.

**Table 3.** Effect of therapy on insomnia symptoms (ISI) during the intervention period.

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>UC+SHUTI</th>
<th>UC+Control</th>
<th>LS Mean Differences (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>574</td>
<td>575</td>
<td>-0.31 (-0.81, 0.18)</td>
<td>0.2120</td>
</tr>
<tr>
<td>Week 2</td>
<td>277</td>
<td>438</td>
<td>-1.43 (-2.00, -0.86)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Week 4</td>
<td>233</td>
<td>384</td>
<td>-3.52 (-4.19, -2.85)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Week 6</td>
<td>195</td>
<td>324</td>
<td>-5.24 (-5.97, -4.51)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Week 8</td>
<td>162</td>
<td>273</td>
<td>-6.18 (-6.96, -5.39)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*Note:* p values are not adjusted for multiplicity and analyses are based on available patient data.
The GoodNight Study (Continued)

A comparison of the LS mean change from baseline to weeks 2, 4, 6, and 8 is presented in Table 4.

**Table 4.** Effect of therapy on change from baseline insomnia symptoms (ISI) during intervention.

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>UC+SHUTi</th>
<th>UC+Control</th>
<th>LS Mean Differences (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of Subjects</td>
<td>LS Mean</td>
<td>Number of Subjects</td>
<td>LS Mean</td>
</tr>
<tr>
<td>Week 2</td>
<td>277</td>
<td>-2.85</td>
<td>438</td>
<td>-1.59</td>
</tr>
<tr>
<td>Week 4</td>
<td>233</td>
<td>-5.97</td>
<td>384</td>
<td>-2.62</td>
</tr>
<tr>
<td>Week 6</td>
<td>195</td>
<td>-7.92</td>
<td>324</td>
<td>-2.87</td>
</tr>
<tr>
<td>Week 8</td>
<td>162</td>
<td>-9.11</td>
<td>273</td>
<td>-3.13</td>
</tr>
</tbody>
</table>

*Note: p values are not adjusted for multiplicity and analyses are based on available patient data.*

Insomnia symptoms were reduced in the UC+SHUTi group in comparison to UC+Control at Weeks 2, 4, 6, and 8 (p<0.0001). Likewise, there was a significant difference between treatment groups in mean change from baseline ISI score beginning at Week 2 (p<0.0001) that was sustained at Weeks 4, 6, and 8 (p<0.0001).
The GoodNight Study (Continued)

Additional Insomnia Analysis: Insomnia Treatment Response and Remission

An analysis of the proportion of study participants deemed treatment responders and remitters was performed using the ISI data. Responders were defined by demonstration of an ISI score reduction of > 7 points clinically. A reduction of 7 or more points is considered optimal to detect treatment responders as it represents a threshold change in insomnia severity category. Remitters were defined as participants achieving an ISI score of < 8, a validated cutoff score for insomnia remission. As defined by the ISI, a score ranging between 0 – 7 indicates ‘no clinically significant insomnia’, a score 8 – 14 indicates ‘mild or subthreshold insomnia’, a score 15 -21 indicates ‘clinical insomnia (moderate severity)’ and a score 22 – 28 indicates “clinical insomnia (severe).”

The proportion of participants in each treatment group deemed treatment responders at week 9, month 6, and month 12 were compared using a chi-square test. Likewise, the proportion of participants in each treatment group deemed treatment remitters at week 9, month 6, and month 12 were compared using a chi-square test.

The proportion of treatment responders identified in each treatment group and their comparison at each timepoint is shown in Table 5. Using criteria of insomnia treatment response (reduction of > 7 points on the ISI from baseline), 62.8% of the UC+SHUTi group were deemed treatment responders from baseline to week 9 compared with 14.0% of the UC+Control group. At the 6 months follow-up, 56.2% of the UC+SHUTi group and 18.9% of the UC+Control group were considered responders. At month 12 follow-up, 59.3% of the UC+SHUTi group and 25.2% of the UC+Control were deemed treatment responders. The difference between treatment groups was significant at all timepoints evaluated (p<0.0001).
The GoodNight Study (Continued)

Table 5. Comparison of proportion of ISI responders (reduction in ISI score > 7 points from baseline) by timepoint.

<table>
<thead>
<tr>
<th>Time of Assessment</th>
<th>UC+SHUTi Proportion</th>
<th>UC+Control Proportion</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>End of Treatment Period</td>
<td>157 (62.8%)</td>
<td>48 (14.0%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>(Week 9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Month 6 Follow-up</td>
<td>127 (56.2%)</td>
<td>53 (18.9%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Month 12 Follow-up</td>
<td>96 (59.3%)</td>
<td>58 (25.2%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Note: p values are not adjusted for multiplicity and analyses are based on available patient data.

A similar pattern was observed for insomnia remitters (Table 6). Using an ISI score of <8 as a cutoff point, 61.6% of the UC+SHUTi group at week 9, 63.7% at month 6, and 63.0% at month 12 were considered insomnia remitters compared with 14.9% of the UC+Control group at week 9, 20.4% at month 6, 25.7% at month 12. The difference between treatment groups (using criteria of either <10 or <8) was significant at every assessment timepoint analyzed (p<0.0001).

Table 6. Comparison of proportion of ISI remitters (ISI score of < 8) by timepoint

<table>
<thead>
<tr>
<th>Time of Assessment</th>
<th>UC+SHUTi Proportion</th>
<th>UC+Control Proportion</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>End of Treatment Period</td>
<td>154 (61.6%)</td>
<td>51 (14.9%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>(Week 9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Month 6 Follow-up</td>
<td>144 (63.7%)</td>
<td>57 (20.4%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Month 12 Follow-up</td>
<td>102 (63.0%)</td>
<td>59 (25.7%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Note: p values are not adjusted for multiplicity and analyses are based on available patient data.
The percentage of participants that achieved a clinically meaningful insomnia treatment response or remission was higher among participants using UC+SHUTi, demonstrating efficacy of UC+SHUTi, compared to UC+Control.

A statistically significance difference in percentage of participants deemed treatment responders at the end of the intervention period was observed in favor of UC+SHUTi over UC+Control. This finding was sustained at follow-up time points (months 6 and 12) following the end of the intervention period. Similarly, a significant difference in the percentage of participants deemed to have achieved insomnia remittance was higher among participants receiving UC+SHUTi than UC+Control. The effect was observed at the end of the intervention period and was sustained 6- and 12-months. Insomnia severity scores of participants deemed to have achieved insomnia remittance were on average, below the clinically validated cutoff score reflecting remission of clinically significant insomnia (score of < 8).

**Additional Insomnia Analysis: Sleep Onset Latency and Wake After Sleep Onset**

Sleep onset latency (SOL) was analyzed using a mixed model repeated measures ANOVA with factors for treatment, time, and treatment*time interaction. This analysis was similar to that done for ISI. Least-Squares (LS) mean SOL values for each treatment group were compared at baseline, at the end of the treatment (week 9), and at month 6, and month 12 follow-up. The analysis included all available data for participants randomized in the trial.
The GoodNight Study (Continued)

Table 7. Effect of therapy on SOL (minutes) by assessment timepoint.

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>UC+SHUTi</th>
<th></th>
<th>UC+Control</th>
<th></th>
<th>LS Mean Differences (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of Subjects</td>
<td>LS Mean</td>
<td>Number of Subjects</td>
<td>LS Mean</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>574</td>
<td>49.12</td>
<td>574</td>
<td>50.00</td>
<td>-0.88 (-5.28, 3.52)</td>
<td>0.6948</td>
</tr>
<tr>
<td>End of Treatment Period (Week 9)</td>
<td>124</td>
<td>25.50</td>
<td>131</td>
<td>47.92</td>
<td>-22.4 (-29.7, -15.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Month 6 Follow-up</td>
<td>161</td>
<td>25.38</td>
<td>201</td>
<td>40.53</td>
<td>-15.1 (-21.2, -9.09)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Month 12 Follow-up</td>
<td>130</td>
<td>20.48</td>
<td>191</td>
<td>37.65</td>
<td>-17.2 (-23.0, -11.3)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Note: p values are not adjusted for multiplicity and analyses are based on available patient data.

A comparison of LS mean SOL values is shown in Table 7. SOL was comparable across treatment groups at baseline (p=0.6948). SOL scores were reduced at week 9 (p<0.0001), month 6 (p<0.0001), and month 12 (p<0.0001) among participants who received UC+SHUTi as compared to UC+Control.

To evaluate the change in SOL over baseline, the change in SOL values from baseline to week 9 and to month 6, and month 12 follow-up were analyzed for each treatment group (Table 8). The average reduction in SOL was greater at week 9 and month 6 for the UC+SHUTi group (mean -22.7 and -22.6 respectively) than the UC+Control group (mean -0.46 and -7.88). Similarly, the average reduction in ISI score was greater at month 12 for the UC+SHUTi group (mean -27.6) than the UC+Control group (mean -10.8). The difference between groups was significant at each timepoint (p<0.0001).
The GoodNight Study (Continued)

Table 8. Effect of therapy on change from baseline (SOL) by assessment timepoint.

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>UC+SHUTi</th>
<th>UC+Control</th>
<th>LS Mean Differences (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of Subjects</td>
<td>LS Mean</td>
<td>Number of Subjects</td>
<td>LS Mean</td>
</tr>
<tr>
<td>End of Treatment Period (Week 9)</td>
<td>124</td>
<td>-22.7</td>
<td>131</td>
<td>-0.46</td>
</tr>
<tr>
<td>Month 6 Follow-up</td>
<td>161</td>
<td>-22.6</td>
<td>201</td>
<td>-7.88</td>
</tr>
<tr>
<td>Month 12 Follow-up</td>
<td>130</td>
<td>-27.6</td>
<td>191</td>
<td>-10.8</td>
</tr>
</tbody>
</table>

Note: p values are not adjusted for multiplicity and analyses are based on available patient data.

An analysis of the proportion of study participants deemed treatment remitters according to their SOL values was also performed. The proportion of participants in each treatment group deemed treatment remitters (defined by demonstration of SOL ≤30 minutes) at week 9, month 6, and month 12 were compared using a chi-square test.

Table 9. Comparison of proportion of SOL remitters (SOL ≤30 minutes) by timepoint.

<table>
<thead>
<tr>
<th>Time of Assessment</th>
<th>UC+SHUTi Proportion</th>
<th>UC+Control Proportion</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>End of Treatment Period (Week 9)</td>
<td>163 (92.6%)</td>
<td>138 (64.5%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Month 6 Follow-up</td>
<td>181 (88.7%)</td>
<td>179 (73.7%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Month 12 Follow-up</td>
<td>131 (90.3%)</td>
<td>164 (75.9%)</td>
<td>0.0005</td>
</tr>
</tbody>
</table>

Note: p values are not adjusted for multiplicity and analyses are based on available patient data.
The GoodNight Study (Continued)

The proportion of treatment remitters identified in each treatment group and their comparison at each timepoint is shown in Table 9. Using criteria of SOL remittance (SOL ≤ 30 minutes), 92.6% of the UC+SHUTi group were deemed treatment remitters from baseline to week 9 compared with 64.5% of the UC+Control group. At the 6 months follow-up, 88.7% of the UC+SHUTi group and 73.7% of the UC+Control group were considered remitters. At month 12 follow-up, 90.3% of the UC+SHUTi group and 72.8% of the UC+Control were deemed remitters. The difference between treatment groups was significant at all timepoints evaluated. The percentage of participants that achieved clinically meaningful remission was higher among participants using UC+SHUTi, demonstrating efficacy of UC+SHUTi, compared to UC+Control.

Wake after sleep onset (WASO) was analyzed using a mixed model repeated measures ANOVA with factors for treatment, time, and treatment*time interaction. This analysis was similar to that done for ISI and SOL. Least-Squares (LS) mean WASO values for each treatment group were compared at baseline, at the end of the treatment (week 9), and at month 6, and month 12 follow-up. The analysis included all available data for participants randomized in the trial.

**Table 10.** Effect of therapy on WASO (minutes) by assessment timepoint.

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>UC+SHUTi</th>
<th>UC+Control</th>
<th>LS Mean Differences (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Subjects</td>
<td>LS Mean</td>
<td>Number of Subjects</td>
<td>LS Mean</td>
<td>Differences (95% CI)</td>
</tr>
<tr>
<td>Baseline</td>
<td>574</td>
<td>49.44</td>
<td>574</td>
<td>50.22</td>
</tr>
<tr>
<td>End of Treatment Period (Week 9)</td>
<td>124</td>
<td>22.95</td>
<td>131</td>
<td>41.80</td>
</tr>
<tr>
<td>Month 6 Follow-up</td>
<td>161</td>
<td>24.04</td>
<td>201</td>
<td>39.67</td>
</tr>
<tr>
<td>Month 12 Follow-up</td>
<td>130</td>
<td>25.86</td>
<td>191</td>
<td>42.34</td>
</tr>
</tbody>
</table>

Note: p values are not adjusted for multiplicity and analyses are based on available patient data.
The GoodNight Study (Continued)

A comparison of LS mean WASO values is shown in Table 10. WASO was comparable across treatment groups at baseline (p=0.7341). WASO values were reduced at week 9 (p<0.0001), month 6 (p<0.0001), and month 12 (p<0.0001) among participants who received UC+SHUTi as compared to UC+Control.

To evaluate the change in WASO over baseline, the change in WASO score from baseline to week 9 and to month 6, and month 12 follow-up were analyzed for each treatment group (Table 11). The average reduction in WASO was greater at week 9 and month 6 for the UC+SHUTi group (mean -28.7 and -27.6 respectively) than the UC+Control group (mean -11.0 and -12.5). Similarly, the average reduction in WASO was greater at month 12 follow-up for the UC+SHUTi group (mean -25.1) than the UC+Control group (mean -9.36). The difference between groups was significant at each timepoint (p<0.0001).

Table 11. Effect of therapy on change from baseline (WASO) by assessment timepoint.

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>UC+SHUTi</th>
<th>UC+Control</th>
<th>LS Mean Differences (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of Subjects</td>
<td>LS Mean</td>
<td>Number of Subjects</td>
<td>LS Mean</td>
</tr>
<tr>
<td>End of Treatment Period (Week 9)</td>
<td>124</td>
<td>-28.8</td>
<td>131</td>
<td>-11.0</td>
</tr>
<tr>
<td>Month 6 Follow-up</td>
<td>161</td>
<td>-27.6</td>
<td>201</td>
<td>-12.5</td>
</tr>
<tr>
<td>Month 12 Follow-up</td>
<td>130</td>
<td>-25.1</td>
<td>191</td>
<td>-9.36</td>
</tr>
</tbody>
</table>

Note: p values are not adjusted for multiplicity and analyses are based on available patient data.

An analysis of the proportion of study participants deemed treatment remitters was also performed. The proportion of participants in each treatment group deemed treatment remitters (defined by demonstration of WASO ≤ 30 minutes) [6] at week 9, month 6, and month 12 were compared using a chi-square test.
The GoodNight Study (Continued)

Table 12. Comparison of proportion of WASO remitters (WASO ≤30 minutes) by timepoint.

<table>
<thead>
<tr>
<th>Time of Assessment</th>
<th>UC+SHUTi Proportion</th>
<th>UC+Control Proportion</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>End of Treatment Period (Week 9)</td>
<td>151 (85.8%)</td>
<td>135 (63.1%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Month 6 Follow-up</td>
<td>165 (80.9%)</td>
<td>159 (65.4%)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Month 12 Follow-up</td>
<td>119 (82.1%)</td>
<td>131 (60.6%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Note: p values are not adjusted for multiplicity and analyses are based on available patient data.

The proportion of treatment remitters identified in each treatment group and their comparison at each timepoint is shown in Table 12. Using criteria of WASO remittance (WASO ≤30 minutes), 85.8% of the UC+SHUTi group were deemed treatment remitters from baseline to week 9 compared with 63.1% of the UC+Control group. At the 6 months follow-up, 80.9% of the UC+SHUTi group and 65.4% of the UC+Control group were considered remitters. At month 12 follow-up, 82.1% of the UC+SHUTi group and 60.6% of the UC+Control were deemed treatment remitters. The difference between treatment groups was significant at all timepoints up to 12 months. The percentage of participants that achieved a clinically meaningful treatment remission was higher among participants using UC+SHUTi, demonstrating efficacy of UC+SHUTi, compared to UC+Control.
The GoodNight Study (Continued)

Effectiveness Outcomes Summary

A summary of the effect of therapy on change from baseline for chronic insomnia outcomes (is provided in Table 13 below).

Table 13. Summary of effect of therapy on change from baseline at the end of the treatment period (week 9) and follow-ups (6 & 12 months).

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Timepoint</th>
<th>UC+SHUTi</th>
<th>UC+Control</th>
<th>LS Mean Differences (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Number of</td>
<td>Number of</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Subjects</td>
<td>Subjects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISI</td>
<td>End of Treatment Period (Week 9)</td>
<td>250</td>
<td>342</td>
<td>-5.78 (-6.50, -5.06)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>Month 6 Follow-up</td>
<td>226</td>
<td>280</td>
<td>-4.31 (-5.09, -3.53)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>Month 12 Follow-up</td>
<td>162</td>
<td>230</td>
<td>-3.59 (-4.46, -2.71)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SOL</td>
<td>End of Treatment Period (Week 9)</td>
<td>124</td>
<td>131</td>
<td>-22.4 (-29.7, -15.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>Month 6 Follow-up</td>
<td>161</td>
<td>201</td>
<td>-15.1 (-21.2, -9.09)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>Month 12 Follow-up</td>
<td>130</td>
<td>191</td>
<td>-17.2 (-23.0, -11.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>WASO</td>
<td>End of Treatment Period (Week 9)</td>
<td>124</td>
<td>131</td>
<td>-18.8 (-24.7, -13.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>Month 6 Follow-up</td>
<td>161</td>
<td>201</td>
<td>-15.6 (-21.1, -10.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>Month 12 Follow-up</td>
<td>130</td>
<td>191</td>
<td>-16.5 (-23.1, -9.91)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Note: *p* values are not adjusted for multiplicity and analyses are based on available patient data.
The GoodNight Study (Continued)

**Secondary Endpoint Analysis: Safety**

Safety was assessed by adverse events. Adverse event reporting was initiated after participant consent and lasted until participation in the study concluded. No participant-reported AEs were identified during the study.

The were no significance differences in AE rate between the UC+SHUTi and UC+Control groups, as no AEs were identified for either treatment group of the study.

Based on these data, SHUTi/Somryst™ can be considered as safe as standard treatment for individuals with chronic insomnia.

The UVA Study

Therapeutic content delivered by Somryst™ was validated in multiple randomized clinical trials including “The UVA Study” RCT sponsored by National Institute of Mental Health (NCT01438697) and conducted at the University of Virginia. Note that the Somryst prescription digital therapeutic was tested as equivalent clinical content, under the name Sleep Healthy Using the Internet (SHUTi), which was accessed via a browser. Somryst delivers equivalent content via a native mobile software application.

The study was designed after previous clinical studies to further evaluate, among other things, Somryst in a population of patients with chronic insomnia.

Study participants (n=303) were between the ages of 21-65, with sleep-onset insomnia and/or sleep maintenance insomnia (>30 minutes for at least 3 nights/week), insomnia symptoms lasting at least 6 months, an average total sleep time $\leq$ 6.5 hours per night, and reported significant distress or impairment in social, occupational, or other areas of functioning caused by sleep disturbances (or associated daytime fatigue).

All study participants received Usual Care (UC) consisting of behavioral treatment, pharmacotherapy and/or self-treatment (e.g., visit to a general practitioner for sleep and/or mood problems, pharmacotherapy (e.g., for sleep and/or mood problems), over-the-counter sleep aids, visit to a sleep specialist, visit to a mental health provider. The Digital Control program provided access to nontailored and fixed digital material about insomnia symptoms; the effect, prevalence, and causes of insomnia; when to see a physician; and basic lifestyle, environmental, and behavioral strategies to improve sleep.
The UVA Study (Continued)

The evaluation of safety and effectiveness of SHUTi to improve sleep, perceived health status, and overall quality of life was evaluated. Participants were randomized 1:1 to 9 weeks of treatment with one of the following:

- UC+SHUTi: Usual Care + SHUTi
- UC+Control: Usual Care + digital patient education for insomnia

Participants in the UC+ SHUTi group (n=151) were asked to complete all six Cores within the 9-week treatment period. Participants randomized to UC+Control (n=152) were able to read the patient education material immediately upon completion of the baseline assessments and could log in to review the material as often as they desired throughout the treatment period. Insomnia symptoms were evaluated for all participants at baseline, the end of the 9-week treatment period and the 6- and 12-month follow-up via the ISI and sleep diaries. Sleep diaries were administered online and collected for a period of 10 days (within a 2-week window), at each assessment time point. Diaries were used to calculate diary-derived variables, including SOL and WASO.

The primary outcome measures of the study were insomnia symptoms, SOL, and WASO measured via ISI and daily sleep diary data at the end of the 9-week treatment period and the 6- and 12-month follow-up.

Endpoint Analysis: Insomnia Severity and Symptomatology

Insomnia symptoms were assessed using the ISI. ISI scores were analyzed using a mixed model repeated measures ANOVA with factors for treatment, time and treatment*time interaction. Least-Squares (LS) mean ISI scores for each treatment group were compared at baseline, at the end of the treatment period (week 9), and at month 6 and month 12 follow ups. The analysis included all available data for participants randomized in the trial.

A comparison of the Least Squares (LS) mean ISI scores for each treatment group and time point is shown in Table 14.
The UVA Study (Continued)

Table 14. Effect of therapy on ISI by assessment timepoint.

<table>
<thead>
<tr>
<th>Time of Assessment</th>
<th>UC+SHUTi</th>
<th>UC+Control</th>
<th>LS Mean Differences (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of Subjects</td>
<td>LS Mean</td>
<td>Number of Subjects</td>
<td>LS Mean</td>
</tr>
<tr>
<td>Baseline</td>
<td>151</td>
<td>17.03</td>
<td>152</td>
<td>17.80</td>
</tr>
<tr>
<td>End of Treatment</td>
<td>133</td>
<td>9.34</td>
<td>142</td>
<td>14.70</td>
</tr>
<tr>
<td>Period (Week 9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Month 6 Follow-up</td>
<td>114</td>
<td>8.65</td>
<td>129</td>
<td>12.29</td>
</tr>
<tr>
<td>Month 12 Follow-up</td>
<td>122</td>
<td>7.60</td>
<td>128</td>
<td>11.60</td>
</tr>
</tbody>
</table>

Note: p values are not adjusted for multiplicity and analyses are based on available patient data.

Insomnia symptoms were comparable across treatment groups at baseline (p=0.0976). LS mean ISI scores were in the clinical insomnia range. Insomnia symptoms were reduced at week 9 (p<0.0001), month 6 (p<0.0001) and month 12 (p<0.0001) among participants who received UC+SHUTi as compared to UC+Control. LS mean ISI scores for the UC+SHUTi group registered in the ‘mild or subthreshold’ insomnia range at week 9 and month 6 follow up, and below the range for ‘mild or subthreshold’ insomnia at month 12 follow up. While insomnia symptoms were reduced for the UC+Control group at each time point, they remained higher in the ‘mild or subthreshold’ insomnia range than the UC+SHUTi group.

To evaluate the change in insomnia symptoms over baseline, the change in ISI score from baseline to week 9, to month 6 and to month 12 were analyzed for each treatment group (Table 15). The average reduction in ISI score was greater at week 9, month 6 and month 12 for the UC+SHUTi group (mean -7.83, -8.52, and -9.57 respectively) than the UC+Control group (mean -2.94, -5.36, and -6.04). The difference between groups was significant at each time point (p<0.0001).
### The UVA Study (Continued)

**Table 15.** Effect of therapy on change from baseline in ISI score by assessment timepoint.

<table>
<thead>
<tr>
<th>Time of Assessment</th>
<th>UC+SHUTi</th>
<th>UC+Control</th>
<th>LS Mean Differences (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>End of Treatment Period (Week 9)</td>
<td>Number of Subjects</td>
<td>LS Mean</td>
<td>Number of Subjects</td>
<td>LS Mean</td>
</tr>
<tr>
<td></td>
<td>133</td>
<td>-7.83</td>
<td>142</td>
<td>-2.94</td>
</tr>
<tr>
<td>Month 6 Follow-up</td>
<td>114</td>
<td>-8.52</td>
<td>129</td>
<td>-5.36</td>
</tr>
<tr>
<td></td>
<td>122</td>
<td>-9.57</td>
<td>128</td>
<td>-6.04</td>
</tr>
</tbody>
</table>

*Note: p values are not adjusted for multiplicity and analyses are based on available patient data.*

Improved insomnia symptom severity was observed in the intent-to-treat study population, demonstrating effectiveness of UC+SHUTi over UC+Control. Participants who received UC+SHUTi showed significant improvement in overall insomnia symptom scores, as well as the within group change in insomnia symptom scores, over UC+Control. Insomnia symptom severity was improved at the end of the treatment period and this effect was maintained to months 6 and 12 following treatment for the participants that received UC+SHUTi.

Participants randomized to UC+SHUTi demonstrated more than a 7-point reduction in insomnia symptom score on average, representing a clinically significant change in insomnia severity. Furthermore, by the end of the treatment period participants receiving SHUTi no longer met the threshold for clinically significant insomnia and on average, maintained a symptom score below the threshold score for clinically significant insomnia at the 12-month follow-up. In contrast, participants randomized to UC+Control maintained an average symptom score above the ‘no clinically significant’ insomnia range on average across all timepoints.
The UVA Study (Continued)

Additional Insomnia Analysis: Insomnia Severity Symptoms During Intervention (Cores 1-6)

An analysis of insomnia severity as measured prior to the initiation of each Core during the treatment period was performed. Summary statistics were calculated to describe insomnia severity among participants receiving UC+SHUTi at each time point. For the UC+Control arm, insomnia severity was not collected from these participants during the treatment period.

Mean ISI scores of participants in the UC+SHUTi arm before and during the intervention period were: 17.026 (±4.0066) at baseline, 15.637 (±4.3784) at Core 1, 15.104 (±4.7371) at Core 2, 12.508 (±4.6484) at Core 3, and 10.963 (±4.8761) at Core 4, 9.673 (±4.5566) at Core 5, and 9.031 (±4.7677) at Core 6. The mean ISI score for the UC+Control arm at baseline was 17.796 (±4.0532).

These data show that UC+SHUTi produced continuous improvements in insomnia symptomology throughout the treatment period.

Additional Insomnia Analysis: Insomnia Treatment Response and Remission

An analysis of the proportion of study participants deemed treatment responders and remitters was performed using the ISI data. Responders were defined by demonstration of an ISI score reduction of > 7 points clinically. A reduction of 7 or more points is considered optimal to detect treatment responders as it represents a threshold change in insomnia severity category [4]. Remitters were defined as participants achieving an ISI score of < 8, a validated cutoff score for insomnia remission [4]. As defined by the ISI, a score ranging between 0 – 7 indicates ‘no clinically significant insomnia’, a score 8 – 14 indicates ‘mild or subthreshold insomnia’, a score 15 -21 indicates ‘clinical insomnia (moderate severity)’ and a score 22 - 28 indicates ‘clinical insomnia (severe)’[4,5].
The UVA Study (Continued)

The proportion of participants in each treatment group deemed treatment responders at week 9, month 6, and month 12 were compared using a chi-square test. Likewise, the proportion of participants in each treatment group deemed treatment remitters at week 9, month 6, and month 12 were compared using a chi-square test.

The proportion of treatment responders identified in each treatment arm and their comparison at each time point is shown in Table 16. Using criteria of insomnia treatment response (reduction of >7 points on the ISI from baseline), 52.6% of the UC+SHUTi arm were deemed treatment responders at week 9 compared with 16.9% of the UC+Control arm. At month 6 follow-up, 59.6% of the UC+SHUTi arm and 35.7% of the UC+Control arm were considered responders. At month 12 follow-up, 69.7% of the UC+SHUTi arm and 43.0% of the UC+Control arm were deemed treatment responders. The difference between treatment groups was significant at all timepoints evaluated.

Table 16. Comparison of proportion of ISI responders (reduction in ISI score > 7 points from baseline) by timepoint.

<table>
<thead>
<tr>
<th>Time of Assessment</th>
<th>UC+SHUTi Proportion</th>
<th>UC+Control Proportion</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>End of Treatment Period</td>
<td>70 (52.6%)</td>
<td>24 (16.9%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>(Week 9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Month 6 Follow-up</td>
<td>68 (59.6%)</td>
<td>46 (35.7%)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Month 12 Follow-up</td>
<td>85 (69.7%)</td>
<td>55 (43.0%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Note: P values are not adjusted for multiplicity and analyses are based on available patient data.

A similar pattern was observed for insomnia remittance (Table 17). Using an ISI score of <8 as a cutoff point, 40.6% of the UC+SHUTi arm at week 9, 49.1% at month 6, and 56.6% at month 12 were considered insomnia remitters compared with 11.3% of the UC+Control arm at week 9, 24.0% at month 6, and 27.3% at month 12. The difference between treatment groups (using criteria of either <10 or <8) was significant at every assessment timepoint analyzed.
The UVA Study (Continued)

Table 17. Comparison of proportion of ISI remitters (ISI score of < 8) by timepoint.

<table>
<thead>
<tr>
<th>Time of Assessment</th>
<th>UC+SHUTi Proportion</th>
<th>UC+Control Proportion</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>End of Treatment Period</td>
<td>54 (40.6%)</td>
<td>16 (11.3%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>(Week 9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Month 6 Follow-up</td>
<td>56 (49.1%)</td>
<td>31 (24.0%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Month 12 Follow-up</td>
<td>69 (56.6%)</td>
<td>35 (27.3%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Note: p values are not adjusted for multiplicity and analyses are based on available patient data.

The percentage of participants that achieved a clinically meaningful insomnia treatment response or remission was higher among participants using UC+SHUTi, demonstrating efficacy of UC+SHUTi, compared to UC+Control.

A statistically significance difference in percentage of participants deemed treatment responders at the end of the intervention period was observed in favor of UC+SHUTi over UC+Control. This finding was sustained at all follow-up time points (months 6 and 12) following the end of the intervention period. Similarly, a significant difference in the percentage of participants deemed to have achieved insomnia remittance was higher among participants receiving UC+SHUTi than UC+Control. The effect was observed at the end of the intervention period and was sustained at 6- and 12-months. Insomnia severity scores of participants deemed to have achieved insomnia remittance were on average, below the clinically validated cutoff score reflecting remission of insomnia (score of < 8).
The UVA Study (Continued)

Additional Insomnia Analysis: Sleep Onset Latency and Wake After Sleep Onset

Sleep onset latency (SOL) was analyzed using a mixed model repeated measures ANOVA with factors for treatment, time, and treatment*time interaction. This analysis was similar to that done for ISI. Least-Squares (LS) mean SOL values for each treatment group were compared at baseline, at the end of the treatment (week 9), and at month 6 and month 12 follow-up. The analysis included all available data for participants randomized in the trial.

Table 18. Effect of therapy on SOL (minutes) by assessment timepoint.

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>UC+SHUTi</th>
<th>UC+Control</th>
<th>LS Mean Differences (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of Subjects</td>
<td>LS Mean</td>
<td>Number of Subjects</td>
<td>LS Mean</td>
</tr>
<tr>
<td>Baseline</td>
<td>151</td>
<td>43.66</td>
<td>149</td>
<td>52.02</td>
</tr>
<tr>
<td>End of Treatment Period (Week 9)</td>
<td>128</td>
<td>24.01</td>
<td>130</td>
<td>41.55</td>
</tr>
<tr>
<td>Month 6 Follow-up</td>
<td>113</td>
<td>24.33</td>
<td>123</td>
<td>36.38</td>
</tr>
<tr>
<td>Month 12 Follow-up</td>
<td>121</td>
<td>21.82</td>
<td>127</td>
<td>33.98</td>
</tr>
</tbody>
</table>

Note: p values are not adjusted for multiplicity and analyses are based on available patient data.

A comparison of LS mean SOL values is shown in Table 18. SOL was reduced at week 9 (p<0.0001), month 6 (p=0.0014), and month 12 (p=0.0020) among participants who received UC+SHUTi as compared to UC+Control. Given a difference in baseline values, the analysis of change in values from baseline was particularly important.

To evaluate the change in SOL over baseline, the change in SOL from baseline to week 9 and to month 6, and month 12 follow-up was analyzed for each treatment group (Table 19). The average reduction in SOL was greater at week 9, month 6 and month 12 for the UC+SHUTi group (mean -21.5, -21.1, and -23.7 respectively) than the UC+Control group (mean -8.84, -13.9, and -16.3). The difference between groups was significant at each timepoint.
The UVA Study (Continued)

**Table 19.** Effect of therapy on change from baseline (SOL) by assessment timepoint.

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>UC+SHUTi</th>
<th></th>
<th>UC+Control</th>
<th></th>
<th>LS Mean Differences (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of Subjects</td>
<td>LS Mean</td>
<td>Number of Subjects</td>
<td>LS Mean</td>
<td></td>
<td></td>
</tr>
<tr>
<td>End of Treatment Period (Week 9)</td>
<td>128</td>
<td>-21.5</td>
<td>129</td>
<td>-8.84</td>
<td>-12.6 (-18.3, -6.92)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Month 6 Follow-up</td>
<td>113</td>
<td>-21.1</td>
<td>121</td>
<td>-13.9</td>
<td>-7.25 (-13.9, -0.62)</td>
<td>0.0323</td>
</tr>
<tr>
<td>Month 12 Follow-up</td>
<td>121</td>
<td>-23.7</td>
<td>124</td>
<td>-16.3</td>
<td>-7.32 (-13.7, -0.90)</td>
<td>0.0255</td>
</tr>
</tbody>
</table>

Note: p values are not adjusted for multiplicity and analyses are based on available patient data.

An analysis of the proportion of study participants deemed treatment remitters was also performed. The proportion of participants in each treatment group deemed treatment remitters (defined by demonstration of SOL ≤30 minutes) at week 9, month 6, and month 12 were compared using a chi-square test [6].

**Table 20.** Comparison of proportion of SOL remitters (SOL ≤30 minutes) by timepoint.

<table>
<thead>
<tr>
<th>Time of Assessment</th>
<th>UC+SHUTi Proportion</th>
<th>UC+Control Proportion</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>End of Treatment Period (Week 9)</td>
<td>114 (89.1%)</td>
<td>85 (63.0%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Month 6 Follow-up</td>
<td>99 (87.6%)</td>
<td>94 (74.6%)</td>
<td>0.0134</td>
</tr>
<tr>
<td>Month 12 Follow-up</td>
<td>112 (92.6%)</td>
<td>100 (78.7%)</td>
<td>0.0021</td>
</tr>
</tbody>
</table>

Note: p values are not adjusted for multiplicity and analyses are based on available patient data.
The UVA Study (Continued)

The proportion of treatment remitters identified in each treatment group and their comparison at each timepoint is shown in Table 20. Using criteria of SOL remittance (SOL ≤30 minutes), 89.1% of the UC+SHUTi group were deemed treatment remitters from baseline to week 9 compared with 63.0% of the UC+Control group. At the 6 months follow-up, 87.6% of the UC+SHUTi group and 74.6% of the UC+Control group were considered remitters. At month 12 follow-up, 92.6% of the UC+SHUTi group and 78.7% of the UC+Control were deemed remitters. The difference between treatment groups was significant at all timepoints evaluated. The percentage of participants that achieved clinically meaningful remission was higher among participants using UC+SHUTi, demonstrating efficacy of UC+SHUTi, compared to UC+Control.

Wake after sleep onset (WASO) was also analyzed using a mixed model repeated measures ANOVA with factors for treatment, time, and treatment*time interaction. This analysis was similar to that done for ISI and SOL. Least-Squares (LS) mean WASO values for each treatment group were compared at baseline, at the end of the treatment (week 9), and at month 6, and month 12 follow-up. The analysis included all available data for participants randomized in the trial.

Table 21. Effect of therapy on WASO (minutes) by assessment timepoint.

<table>
<thead>
<tr>
<th>Time of Assessment</th>
<th>UC+SHUTi</th>
<th></th>
<th>UC+Control</th>
<th></th>
<th>LS Mean Differences (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of Subjects</td>
<td>LS Mean</td>
<td>Number of Subjects</td>
<td>LS Mean</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>151</td>
<td>46.19</td>
<td>149</td>
<td>49.11</td>
<td>-2.92 (-11.5, 5.69)</td>
<td>0.5050</td>
</tr>
<tr>
<td>End of Treatment Period (Week 9)</td>
<td>128</td>
<td>22.14</td>
<td>130</td>
<td>39.30</td>
<td>-17.2 (-24.3, -9.97)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Month 6 Follow-up</td>
<td>113</td>
<td>22.98</td>
<td>123</td>
<td>35.06</td>
<td>-12.1 (-19.2, -5.01)</td>
<td>0.0009</td>
</tr>
<tr>
<td>Month 12 Follow-up</td>
<td>121</td>
<td>18.46</td>
<td>127</td>
<td>31.14</td>
<td>-12.7 (-18.9, -6.51)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Note: p values are not adjusted for multiplicity and analyses are based on available patient data.
The UVA Study (Continued)

A comparison of LS mean WASO values is shown in Table 21. WASO was comparable across treatment groups at baseline (p=0.5050). WASO scores were reduced at week 9 (p<0.0001), month 6 (p=0.0009), and month 12 (p<0.0001) among participants who received UC+SHUTi as compared to UC+Control.

To evaluate the change in WASO over baseline, the change in WASO from baseline to week 9 and to month 6, and month 12 follow-up were analyzed for each treatment group (Table 22). The average reduction in WASO was greater at week 9, month 6, and month 12 for the UC+SHUTi group (mean -24.9, -23.9, -28.4 respectively) than the UC+Control group (mean -8.46, -12.9, and -16.8). The difference between groups was significant at all post-baseline timepoints (p<0.001).

**Table 22.** Effect of therapy on change from baseline (WASO) by assessment timepoint.

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>UC+SHUTi</th>
<th>UC+Control</th>
<th>LS Mean Differences (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>End of Treatment Period (Week 9)</td>
<td>Number of Subjects</td>
<td>LS Mean</td>
<td>Number of Subjects</td>
<td>LS Mean</td>
</tr>
<tr>
<td>Month 6 Follow-up</td>
<td>113</td>
<td>-23.9</td>
<td>121</td>
<td>-12.9</td>
</tr>
<tr>
<td>Month 12 Follow-up</td>
<td>121</td>
<td>-28.4</td>
<td>124</td>
<td>-16.8</td>
</tr>
</tbody>
</table>

Note: p values are not adjusted for multiplicity and analyses are based on available patient data.

An analysis of the proportion of study participants deemed treatment remitters was also performed. The proportion of participants in each treatment group deemed treatment remitters (defined by demonstration of WASO ≤ 30 minutes) [6] at week 9, month 6, and month 12 were compared using a chi-square test.
The UVA Study (Continued)

Table 23. Comparison of proportion of WASO remitters (WASO ≤30 minutes) by timepoint.

<table>
<thead>
<tr>
<th>Time of Assessment</th>
<th>UC+SHUTi Proportion</th>
<th>UC+Control Proportion</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>End of Treatment Period (Week 9)</td>
<td>107 (83.6%)</td>
<td>83 (61.5%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Month 6 Follow-up</td>
<td>98 (86.7%)</td>
<td>88 (69.8%)</td>
<td>0.0018</td>
</tr>
<tr>
<td>Month 12 Follow-up</td>
<td>111 (91.7%)</td>
<td>92 (72.4%)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Note: p values are not adjusted for multiplicity and analyses are based on available patient data.

The proportion of treatment remitters identified in each treatment group and their comparison at each timepoint is shown in Table 23. Using criteria of WASO remittance (WASO ≤30 minutes), 83.6% of the UC+SHUTi group were deemed treatment remitters from baseline to week 9 compared with 61.5% of the UC+Control group. At the 6 months follow-up, 86.7% of the UC+SHUTi group and 69.8% of the UC+Control group were considered remitters. At month 12 follow-up, 91.7% of the UC+SHUTi group and 72.4% of the UC+Control were deemed treatment remitters. The difference between treatment groups was significant at all timepoints evaluated. The percentage of participants that achieved a clinically meaningful treatment remission was higher among participants using UC+SHUTi, demonstrating efficacy of UC+SHUTi, compared to UC+Control.
**The UVA Study (Continued)**

**Effectiveness Outcomes Summary**

A summary of effect of therapy on change from baseline outcomes is provided in Table 24 below.

**Table 24.** Summary of effect of therapy on change from baseline at End of Treatment (Week 9) and Follow-ups (6 & 12 months).

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Timepoint</th>
<th>UC+SHUTi</th>
<th>UC+Control</th>
<th>LS Mean Differences (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Number of Subjects</td>
<td>LS Mean</td>
<td>Number of Subjects</td>
<td>LS Mean</td>
</tr>
<tr>
<td>ISI</td>
<td>End of Treatment Period (Week 9)</td>
<td>133</td>
<td>-7.83</td>
<td>142</td>
<td>-2.94</td>
</tr>
<tr>
<td></td>
<td>Month 6 Follow-up</td>
<td>114</td>
<td>-8.52</td>
<td>129</td>
<td>-5.36</td>
</tr>
<tr>
<td></td>
<td>Month 12 Follow-up</td>
<td>122</td>
<td>-9.57</td>
<td>128</td>
<td>-6.04</td>
</tr>
<tr>
<td>SOL</td>
<td>End of Treatment Period (Week 9)</td>
<td>128</td>
<td>-21.5</td>
<td>130</td>
<td>-8.84</td>
</tr>
<tr>
<td></td>
<td>Month 6 Follow-up</td>
<td>113</td>
<td>-21.1</td>
<td>123</td>
<td>-13.9</td>
</tr>
<tr>
<td></td>
<td>Month 12 Follow-up</td>
<td>121</td>
<td>-23.7</td>
<td>127</td>
<td>-16.3</td>
</tr>
<tr>
<td>WASO</td>
<td>End of Treatment Period (Week 9)</td>
<td>128</td>
<td>-24.9</td>
<td>130</td>
<td>-8.46</td>
</tr>
<tr>
<td></td>
<td>Month 6 Follow-up</td>
<td>113</td>
<td>-23.9</td>
<td>123</td>
<td>-12.9</td>
</tr>
<tr>
<td></td>
<td>Month 12 Follow-up</td>
<td>121</td>
<td>-28.4</td>
<td>127</td>
<td>-16.8</td>
</tr>
</tbody>
</table>

**Note:** p values are not adjusted for multiplicity and analyses are based on available patient data.
The UVA Study (Continued)

Secondary Endpoint Analysis: Safety

Recording and reporting of unanticipated problems and adverse events was initiated once a participant signed informed consent and ended upon completion of participation in the protocol. No AEs were identified for either treatment group of the study, and thus, no significant differences in AE rate between the UC+SHUTi and UC+Control groups were found. Based on these data, SHUTi/Somryst™ can be considered as safe as standard treatment for individuals with insomnia.

Citations


INTRODUCTION

Chronic insomnia is a significant public health problem, due not only to the disease itself, but its tendency to co-occur with other serious medical and psychiatric disorders. Insomnia also poses a significant economic burden on patients and healthcare organizations, with direct and indirect costs in the United States estimated to exceed US$100 billion each year.

Prescription digital therapeutics (PDTs) are a new class of software-based disease treatments that deliver evidence-based therapeutic interventions on smartphones or tablets. PDTs are clinically validated and authorized for use by the U.S. Food and Drug Administration based on rigorous clinical trial data. PDTs can be used alone or in combination with drugs and are being developed for a wide range of medical conditions including chronic insomnia.

These analyses evaluated health care-related utilization before and after initiation of treatment with a PDT that delivers cognitive behavioral therapy for insomnia (CBT-I) to adults with chronic insomnia (Somryst®, previously called SHUTi). The PDT provides a digital version of CBT-I to patients who are clinician-supervised in outpatient settings. Content is delivered via six interactive treatment modules designed to parallel the traditional, face-to-face delivery and structure of CBT-I sessions during the 9-week prescription period.

OBJECTIVE

To examine the impact of a PDT on healthcare resource utilization (HCRU) in patients with chronic insomnia by direct comparison of HCRU and selected clinical outcomes before and after PDT initiation.

MATERIALS AND METHODS

We conducted a pre/post analysis of claims data by comparing two-year pre- and post-index healthcare resource utilization (HCRU) in U.S. patients with self-identified sleep problems who activated the PDT between February 1, 2012 and December 31, 2018.

The index date was the date of PDT initiation, pre-index date was 24 months before the index date and the post-index date was 24 months after the index date. HCRU categories assessed were: hospitalizations, treat-and-release emergency department (ED) visits, ambulatory surgical center (ASC) visits, hospital outpatient department (HOPD) visits, office visits, and use of sleep medications.

LIMITATIONS

This study is subject to the limitations of administrative claims data: coding errors that include under-coding, over-coding, not coding at the highest level of specificity, and unbundling.

RESULTS (PRE- VS POST-INDEX 24 MONTHS)

252 patients were analyzed; mean age = 54.2 yrs, female = 57.5%. Mean Charlson co-morbidity index score: 0.8 (std dev: 1.48)

Post-index events were reduced compared to the pre-index period for ED visits (-56.2%; P=0.001), hospitalizations (-20.9%; P=0.400), sleep medication use (-8.9%; P=0.377), hospital outpatient services (-8.3%; P=0.522), and ambulatory surgical center services (-6.7%; P=0.695). Office visits in the post-index period were slightly higher compared to pre-index period (+0.7%; P=0.891).

CONCLUSION

Treatment with a PDT delivering digital CBT-I in a real-world population of patients with chronic insomnia was associated with clinically meaningful reductions in health-related services.

References: