Mass General Brigham

Research Consent Form
General Consent Form Template
Version Date: February 2021

Subject Identification

Protocol Title: Efficacy of Suvorexant in Patients with Effectively Treated Restless Legs Syndrome and Persistent Chronic Insomnia: A Randomized Placebo-Controlled Crossover Trial

Principal Investigator: John W Winkelman MD PhD

Site Principal Investigator:

Description of Subject Population: Patients with Effectively Treated Restless Legs Syndrome and Persistent Chronic Insomnia

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

Key Information

Taking part in this research study is up to you. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. Your decision won't change the medical care you get within Mass General Brigham now or in the future.

The following key information is to help you decide whether or not to take part in this research study. We have included more details about the research in the Detailed Information section that follows the key information.

Why is this research study being done?

The purpose of the study is to learn about the safety and effectiveness of oral (taken by mouth) suvorexant (Belsomra®) in improving sleep quality and sleep quantity in patients who have treated restless legs syndrome (RLS).

How long will you take part in this research study?

It will take you about 12 weeks (about 3 months) to complete the study; during this time, you will be asked to make 5 study visits. All study visits will occur remotely over Zoom. In addition, a member of the study staff will call you 2 times in addition to the initial phone call that you already had with the study team.

What will happen if you take part in this research study?

If you decide to join this research study, you will be asked to complete: sleep diaries, home actigraphy, questionnaires, 2 phone calls, and 5 visits. During those visits, you will speak with the study team and complete questionnaires.

Why might you choose to take part in this study?

We cannot promise any benefits to you from taking part in this research study. Others with treated RLS and insomnia may benefit in the future from what we learn in this study. Additionally, you will be compensated up to $250 for your participation in this study.

Why might you choose NOT to take part in this study?

Taking part in this research study has some risks and requirements that you should consider carefully.

Important risks and possible discomforts to know about include side effects of the study medication, suvorexant. Side effects include: sleepiness or drowsiness during the day, not thinking clearly, acting strangely, sleep-walking, temporary weakness, diarrhea, dry mouth, upper respiratory tract infection, headache, dizziness, abnormal dreams, and cough.

A detailed description of side effects, risks, and possible discomforts can be found later in this consent form in the section called “What are the risks and possible discomforts from being in this research study?”

Another thing to consider is the time commitment for completing daily sleep diaries, which will be sent to your email address each morning and submitted back to us online.

What other treatments or procedures are available for your condition?

You do not have to take part in this research study to receive treatment for your disease. There are other currently-approved treatments for insomnia, and the study doctor can tell you what other options are available to you. There are more details on approved treatments for insomnia later in this form.

If you have questions or concerns about this research study, whom can you call?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

John Winkelman, MD PhD is the person in charge of this research study. You can call him at **617-643-9101** from 9 am to 5 pm on weekdays. He is available 24 hours a day, 7 days a week, by paging him at Massachusetts General Hospital, 617-726-2000.

If you have questions about the scheduling of appointments or study visits, call **Jordana Zackon** at **617-643-6026** or email jzackon@mgh.harvard.edu.

If you want to speak with someone **not** directly involved in this research study, please contact the Mass General Brigham IRB office. You can call them at 857-282-1900.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research
- Any pressure to take part in, or to continue in the research study

Detailed Information

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov,* as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Why is this research study being done?

The purpose of the study is to learn about the safety and effectiveness of oral (taken by mouth) suvorexant (Belsomra®) in improving sleep quality and sleep quantity in patients who have treated RLS. We are asking you to take part in this research study because you have RLS and significant sleep disruption. There is evidence that sleep disturbances are common in patients with treated RLS.

In this study we are comparing suvorexant to placebo. A placebo is a pill that looks exactly like the study drug, but it does not have any active drug in it. You will receive both suvorexant and placebo during the study. You will receive one medication during the first four-week treatment period, and the other during the second four-week treatment period. You will not be informed as to which medication you are taking at various points throughout the study. We use placebos in research studies to learn if the effects seen in research subjects are truly from the study drug or from other reasons. Throughout this form, the phrase "study drug" applies to both treatments that you could get: suvorexant and placebo.

Suvorexant (Belsomra®) is approved by the U.S. Food and Drug Administration (FDA) for the treatment of insomnia in patients 18 years of age and older. This study is investigating the use of suvorexant specifically in a population of patients with treated RLS.

Suvorexant (Belsomra®) is manufactured by Merck & Co., Inc.

We hope to enroll 90 subjects between the ages of 25 and 85.

Who will take part in this research?

This is a pilot study. A pilot study is done on a small group of subjects to learn if the study drug will be effective and safe, before the study drug is given to a larger group of subjects.

In this study, we hope to enroll 90 subjects between the ages of 25 and 85, with treated RLS and insomnia.

This study is being funded by Merck & Co., Inc.

What will happen in this research study?

The study has the following phases:

Screening Phase

- Screening Period (two weeks): You have already completed the Telephone Screen and the two-week period that proceeds the virtual Screening Visit (including the completion of two weeks of sleep diaries, which will be reviewed at the Screening Visit). At the Screening Visit, you will be informed of all the study procedures and evaluated for eligibility.
- At the Screening Visit, if you wish to participate in the study, we will ask you to stop taking any medications that are considered exclusionary. These include:
    - Strong inhibitors of CYP3A
        - Ketoconazole, itraconazole, posaconazole, clarithromycin, nefazodone, ritonavir, saquinavir, nelfinavir, indinavir, boceprevir, telaprevir, telithromycin, conivaptan
    - *Subjects may continue, but a maximum dose of 10 mg will typically be given for subjects taking moderate CYP3A inhibitors
        - Amprenavir, aprepitant, atazanavir, ciprofloxacin, diltiazem, erythromycin, fluconazole, fosamprenavir, grapefruit juice, imatinib, verapamil
    - In certain cases, subjects on moderate CYP3A inhibitors may be administered 20 mg of suvorexant if the study doctor determines that side effects at 10 mg do not preclude an increase in dose. In these cases, an additional safety phone call will be performed after 1 week at the higher dose (20 mg) in both treatment periods.

- At the Screening Visit, you will meet with the study doctor (approximately 30 minutes). The doctor will ask you questions about your medical history, sleep history, psychiatric history, RLS, sleep quality, and medications.
- If you are a woman who is able to become pregnant, a urine pregnancy test will be done. If you are pregnant, you will not be allowed to take part in the study. You will need to have this test performed at an affiliated site or a satellite clinic. We will pay for this test.

- After the Screening Visit, the study doctor will continue to evaluate whether you are eligible for this study over another two-week period. You will be asked to complete another two weeks of sleep diaries. We will also mail you a Phillips Actiwatch Spectrum Plus. We will ask you to wear this device on your non-dominant wrist both day and night at all times except when showering. After two weeks of use, we will ask you to mail the actiwatch back to us. We will pay for the postage fees.

Study Drug

We will assign you by chance to one of two study groups. One out of every two people will receive suvorexant up to 20 mg/night, and the rest of participants will receive placebo (contains no active drug). You, the study doctor, and the study staff will not know which group you are in, but we can find out this information if we need it.

Throughout this form the phrase "study drug" applies to suvorexant and placebo. The study drug will be provided in a single capsule of suvorexant or placebo. It is important that you follow your study doctor's or the study staff's instructions on when and how to take the study drug. The study drug will be provided in child-resistant bottles.

Start of Treatment 1 (Week 0)

- At this virtual visit, the study doctor will determine whether you are still eligible to participate in the study.
- You will meet with the study doctor to discuss medications, sleep quality, health conditions, and the details of your participation in the study. The study doctor will discuss all possible side effects from the study drug, and you will be able to ask any questions.
- You will be asked to complete questionnaires (approximately 20 minutes). This information is kept confidential and will only be used for study purposes.
- **You will be mailed a 14-day supply of study drug at this visit** to be taken at night before bed, and you will be provided with instructions on how to store, how/when to take, and any risks associated with, the study drug. The study drug may be suvorexant or placebo, you will be assigned randomly to either group, and neither the study staff nor you will know which one you are taking.
- **You will also be mailed an additional 3-week supply of study drug.** During Interim Phone Call 1, you will be provided with instructions on how/when to take this additional medication.
- You will also be mailed an actiwatch with the medication.

Interim Phone Call 1 (Week 1)

- During week 1, you will be contacted via phone by the study doctor. The study doctor will discuss with you the effectiveness of the study drug and ask about any side effects you may have experienced. If you did not experience any side effects during the first week, and the 10-mg dose was ineffective, your dose will be increased to 20 mg (i.e. the doctor will instruct you to take two 10-mg pills nightly).

End of Treatment 1 (Week 4)

- Prior to this virtual visit, you will be asked to complete 2 weeks of sleep diaries and actigraphy.
- You will meet with the study doctor to discuss your medications, sleep quality, health conditions, and mood, and you will be able to ask any questions. The study doctor will discuss with you the effectiveness of the study drug and inquire about any side effects you may have experienced.
- You will be asked to complete questionnaires (approximately 20 minutes). This information is kept confidential and will only be used for study purposes.
- You will be asked to show the study doctor all remaining medication over Zoom.
- You will be asked to mail the actiwatch back to the study team following this visit.
- At this point, you will begin a two-week washout phase, meaning that you will not be taking any medication until after the next visit.

Start of Treatment 2 (Week 6)

- You will meet with the study doctor to discuss medications, sleep quality, health conditions, and the details of your participation in the study. The study doctor will discuss all possible side effects from the study drug, and you will be able to ask any questions.
- **You will be mailed a 14-day supply of study drug at this visit** to be taken at night before bed, and you will be provided with instructions on how to store, how/when to take, and any risks associated with, the study drug. The study drug may be suvorexant or placebo, you will be assigned randomly to either group, and neither the study staff nor you will know which one you are taking.
- **You will also be mailed an additional 3-week supply of study drug.** During Interim Phone Call 2, you will be provided with instructions on how/when to take this additional medication.
- You will also be mailed an actiwatch with the medication.

Interim Phone Call 2 (Week 7)

- During week 7, you will be contacted via phone by the study doctor. The study doctor will discuss with you the effectiveness of the study drug and ask about any side effects you may have experienced. If you did not experience any side effects during the first week, and the 10-mg dose was ineffective, your dose will be increased to 20 mg (i.e. the doctor will instruct you to take two 10-mg pills nightly).

End of Treatment 2 (Week 10)

- Prior to this virtual visit, you will be asked to complete 2 weeks of sleep diaries and actigraphy.
- You will meet with the study doctor to discuss your medications, sleep quality, health conditions, and mood, and you will be able to ask any questions. The study doctor will discuss with you the effectiveness of the study drug and inquire about any side effects you may have experienced.
- You will be asked to complete questionnaires (approximately 20 minutes). This information is kept confidential and will only be used for study purposes.
- You will be asked to show the study doctor all remaining medication over Zoom.
- You will be asked to mail the actiwatch back to the study team following this visit.

Remote Visits

During this study we may need to make changes to study visits and procedures to comply with public health efforts to address COVID-19 (coronavirus). We may need to adjust the study visit schedule and/or research procedures as a result of study site restrictions. We will contact you about any such changes that may arise.

Remote visits will be conducted either over the phone or by Zoom. During these visits, someone from the study staff will contact you.

Video Conferencing

Study staff will provide you information on how to access the video conferencing platform. We will launch the video conferencing in a private and secure area. To protect your privacy we ask that you do not take screenshots, photographs, or recordings of any kind with any electronic equipment.

We would like to remind you that a video meeting is similar to us visiting you at home. We may learn more about your home and the people living with you than we would during a visit at the hospital. For example, we may learn information from you that must be reported to public health or public safety authorities. We are required by law to report known or suspected child or elder abuse. If we make such report, the public health and safety authorities can use the information as they see fit and may end up sharing it with other government agencies. Please ask the research staff if you have any questions about this prior to your video visit.

Early Withdrawal
You may withdraw from this study at any time. If you wish to stop taking part in the study for any reason, please contact the study staff. We will give you instructions to gradually stop taking the study drug, if necessary. Depending on the point at which you withdraw from the study, we may ask you to participate in a final visit.

The study doctor may decide to end your participation in the study. This might happen if you have changes in your health, if you do not follow instructions, or if you do not attend the study visits.

General Information
All of the information collected in this study will only be used for research and will not be placed in your medical records. To protect your privacy, we will use a unique identification number on your study forms instead of your name or address. The study staff will keep a list that matches your unique identification number to your name, but we will not share this list with anyone.

How may we use and share your samples and health information for other research?

The information we collect in this study may help advance other research. If you join this study, we may remove all information that identifies you (for example, your name, medical record number, and date of birth) and use these de-identified samples and data in other research. It won't be possible to link the information or samples back to you. Information and/or samples may be shared with investigators at our hospitals, at other academic institutions or at for-profit, commercial entities. You will not be asked to provide additional informed consent for these uses.

Will you get the results of this research study?

No. The research study we are doing is only a stepping stone in understanding **[condition].** Therefore, no information about the results of this research study or the results of your individual participation in the research study will be given to you or your doctor. Tests done for the research using your samples will not be useful in directing your medical treatment. The results of the tests will not be placed in your medical record.

What are the risks and possible discomforts from being in this research study?

RISKS ASSOCIATED WITH THE STUDY DRUG

All drugs may cause side effects. The most commonly reported side effects associated with suvorexant in research studies include:

- sleepiness or drowsiness during the day
- headache
- dizziness

Less-common side effects include:

- diarrhea
- dry mouth
- upper respiratory tract infection
- abnormal dreams
- cough

Rare, but serious side effects include:

- temporary weakness in your legs or inability to move or talk, otherwise known as cataplexy
- not thinking clearly
- acting strangely, confused, or upset
- "sleep-walking" or doing other activities during sleep, such as eating, talking, having sex, or driving a car

Suvorexant may cause a change (increase or decrease) in the effect of some other drugs. If you are taking other drugs while you are participating in this study, the study doctor will explain whether suvorexant may have an effect on those drugs. If necessary, the study doctor may adjust your drug dose.

There may be other risks and side effects to suvorexant that are not known at this time. You will be notified of any new significant findings that might affect your willingness to continue to participate in this study.

Due to the possibility of dizziness or drowsiness, you must be cautious when operating a vehicle or heavy equipment while in this study. You should wait to operate a vehicle or heavy equipment until you have experience using suvorexant.

Your condition may remain the same or worsen while you are taking part in this study.

If you experience any side effects, you should contact John Winkelman, MD, PhD (the study doctor) immediately at one of the contact numbers listed in the study contacts section near the beginning of this form.

RISKS ASSOCIATED WITH CONSUMING ALCOHOL The use of suvorexant and alcohol are contraindicated due to potential serious side effects, including drowsiness, dizziness, and diminished judgement and coordination. If you consume alcohol while taking the study drug and experience any side effects, contact John Winkelman, MD, PhD (the study doctor) immediately.

REPRODUCTIVE RISKS
You cannot take part in this study if you are pregnant or nursing an infant. If you are a woman who is able to become pregnant, you must use birth control throughout the study. Acceptable methods of birth control include:

- hormonal contraceptives (birth control pills, patches, implants, or injections)
- spermicide and barrier (barriers include condoms and diaphragms)
- intrauterine device (IUD)
- spousal/partner sterility (unable to father or mother a child)
- abstinence (If you are practicing abstinence, you must agree to continue abstinence or to use an acceptable method of contraception, as noted above, if sexual activity begins.)

It is possible that some hormonal contraceptives (birth control pills, hormonal implants or hormonal injections) may be made less effective because of the use of suvorexant. If necessary, your study doctor will discuss alternatives or additional non-hormonal methods of birth control that you should use while you are taking part in the study. If you are taking birth control pills, you should report to your study doctor any change in your bleeding patterns.

If you are a female who is able to become pregnant, you will have periodic pregnancy tests throughout the research study. If these tests show that you are pregnant, you will not be able to enter and stay in the study. You must accept the risk that pregnancy could still result even though

you are using a reliable method of birth control. If you become pregnant during the study, you must inform the study doctor immediately.

If you become pregnant during this study, you will be discontinued from the study and the study drug will be stopped immediately. Your study doctor will explain the potential hazards that may affect the fetus and possible alternatives, which may include ending the pregnancy.

RISKS ASSOCIATED WITH TAPERING OFF OF MEDICATIONS

A number of risks associated with tapering off prescribed medications can occur, including a return of symptoms for which the medication is prescribed, and medication specific withdrawal effects. The study doctor will discuss any of these risks with you.

What are the possible benefits from being in this research study?

You may not benefit from taking part in this study. You will receive suvorexant at a point during the study, which may help your condition. You may benefit from the sleep diaries, actigraphy, urine tests, review of your symptoms, and regular discussions with the study doctor. Your taking part in this study may help other people with insomnia and RLS by adding to the knowledge about this drug, and whether it is a beneficial treatment.

What other treatments or procedures are available for your condition?

You do not have to take part in this research study to receive treatment for your disease. There are other currently approved treatments for insomnia, and the study doctor can tell you what other options are available to you.

The study drug is available by prescription without participating in this study. Other medications approved for the treatment of insomnia include: Zolpidem (Ambien), Zaleplon (Sonata), Ramelteon (Rozerem), Eszopiclone (Lunesta), Doxepine (Silenor), some benzodiazepines, and some antidepressants.

Can you still get medical care within Mass General Brigham if you don't take part in this research study, or if you stop taking part?

Yes. Your decision won't change the medical care you get within Mass General Brigham now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should you do if you want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

Also, it is possible that we will have to ask you to drop out of the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

Will you be paid to take part in this research study?

You will be paid for each study visit ($50 for the Screening Visit and $25 for each subsequent visit) and for the 1-week and 7-week phone calls ($25 each). You will receive a completion bonus when you have completed the study in its entirety ($50 at the End of Treatment 2 Visit).

We may be using an approved, outside vendor (Forte Research) to make these payments to you via a reloadable credit card-based system, called Forte Payments. This secure system is similar to a gift card or credit card. If you are paid by this system, you will be given a Forte Payments Visa card when you enroll in the study. Once the card is activated, the study team will add a payment after each paid visit you complete. You may use the card anywhere Visa cards are accepted, such as at a grocery store.

We may use your samples and information to develop a new product or medical test to be sold. The Sponsor, hospital, and researchers may benefit if this happens. There are no plans to pay you if your samples or information are used for this purpose.

What will you have to pay for if you take part in this research study?

You will not have to pay anything to take part in this study. The study drug, medical care, and all tests and procedures that are done as part of the research will be paid for by study funds. If you have any questions about costs to you that may result from taking part in the research, please speak with the study doctors and study staff. If necessary, we will arrange for you to speak with someone in Patient Financial Services about these costs.

What happens if you are injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the beginning of this consent form.

If you take part in this research study, how will we protect your privacy?

Federal law requires Mass General Brigham to protect the privacy of health information and related information that identifies you. We refer to this information as "identifiable information."

In this study, we may collect identifiable information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable information and why they may need to do so:

- Mass General Brigham researchers and staff involved in this study
- The sponsor(s) of the study, and people or groups it hires to help perform this research or to audit the research
- Other researchers and medical centers that are part of this study
- The Mass General Brigham ethics board or an ethics board outside Mass General Brigham that oversees the research

- A group that oversees the data (study information) and safety of this study
- Non-research staff within Mass General Brigham who need identifiable information to do their jobs, such as for treatment, payment (billing), or hospital operations (such as assessing the quality of care or research)
- People or groups that we hire to do certain work for us, such as data storage companies, accreditors, insurers, and lawyers
- Federal agencies (such as the U.S. Department of Health and Human Services (DHHS) and agencies within DHHS like the Food and Drug Administration, the National Institutes of Health, and the Office for Human Research Protections), state agencies, and foreign government bodies that oversee, evaluate, and audit research, which may include inspection of your records
- Public health and safety authorities, if we learn information that could mean harm to you or others (such as to make required reports about communicable diseases or about child or elder abuse)
- Other:

Some people or groups who get your identifiable information might not have to follow the same privacy rules that we follow and might use or share your identifiable information without your permission in ways that are not described in this form. For example, we understand that the sponsor of this study may use your identifiable information to perform additional research on various products or conditions, to obtain regulatory approval of its products, to propose new products, and to oversee and improve its products' performance. We share your identifiable information only when we must, and we ask anyone who receives it from us to take measures to protect your privacy. The sponsor has agreed that it will not contact you without your permission and will not use or share your identifiable information for any mailing or marketing list. However, once your identifiable information is shared outside Mass General Brigham, we cannot control all the ways that others use or share it and cannot promise that it will remain private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your identifiable information. Your permission to use and share your identifiable information does not expire.

The results of this research study may be published in a medical book or journal, or used to teach others. However, your name or other identifiable information **will not** be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your identifiable information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your identifiable information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others, and such information may continue to be used for certain purposes, such as to comply with the law or maintain the reliability of the study.

You have the right to see and get a copy of your identifiable information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.
- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me.

Signature of Subject:

I give my consent to take part in this research study and agree to allow my health information to be used and shared as described above.

Subject	Date	Time (optional)

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the study subject.
- I have answered all questions about this research study to the best of my ability.

Study Doctor or Person Obtaining Consent	Date	Time (optional)

Consent Form Version: 2

Consent Form Created on: 2/18/2021