New York State Psychiatric Institute

Institutional Review Board

October 07, 2016

To: Dr. Franklin Schneier

From: Dr. Edward Nunes, Co-Chairman
Dr. Laurence Greenhill, Co-Chairman

Subject: Approval Notice: CONTINUATION

Your protocol # **6856** entitled: **VILAZODONE FOR SEPARATION ANXIETY DISORDER IN ADULTS**
Protocol version date 10/07/2016 and consent forms have been approved by the New York State Psychiatric Institute - Columbia University Department of Psychiatry Institutional Review Board from **October 21, 2016 to October 20, 2017.** (Reviewed at the Full Board meeting on September 26, 2016.)

Consent requirements:
☐ Not applicable:
☐ 45CFR46.116 (d) waiver or alteration of consent for the telephone interview
√ Signature by the person(s) obtaining consent is required to document the consent process
☐ Documentation of an independent assessment of the participant's capacity to consent is also required.

Approved for recruitment of subjects who lack capacity to consent: √ No ☐ Yes

Field Monitoring Requirements: √ Routine ☐Special: _____

✓ Only copies of consent documents that are currently approved by the IRB may be used to obtain consent for participation in this study.
✓ A progress report and application for continuing review is required 2 months prior to the expiration date of IRB approval.
✓ Changes to this research may not be initiated without the review and approval of the IRB except when necessary to eliminate immediate hazards to participants.
✓ All serious and/or unanticipated problems or events involving risks to subjects or others must be reported immediately to the IRB. Please refer to the PI-IRB website at http://irb.nyspi.org for Adverse Event Reporting Procedures and additional reporting requirements.

Cc: RFMH Business Office (Forest Labs)

Encl: CF, recruitment materials, HIPAA

EN/LG/alw

Signed copy on file at IRB

Protocol Title:
Vilazodone for Separation Anxiety Disorder in Adults

Version Date:
10/07/2016

Protocol Number:
6856

First Approval:
11/12/2013

Clinic:
Anxiety Disorders Clinic

Expiration Date:
10/20/2016

Contact Principal Investigator:
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Co-Investigator(s):
Raphael Campeas, MD

Research Chief:
B. Timothy Walsh, MD

Cover Sheet

Choose from the following that is applicable to your study
I am submitting an annual continuation without modifications

Division & Personnel

Division

What Division/Department does the PI belong to?
Clinical Therapeutics
Within the division/department, what Center or group are you affiliated with, if any?
Anxiety Disorders Clinic

Unaffiliated Personnel

List investigators, if any, who will be participating in this protocol but are not affiliated with New York State Psychiatric Institute or Columbia University. Provide: Full Name, Degrees and Affiliation.
None

Application for Continuation of Research

Status

Current Status of Study:
Subject enrollment is ongoing.

Summary of Experiences to Date

Please provide a summary of scientific progress of the study and the experience of research participants, to date. This requirement is designed to allow for the investigator and the IRB to reassess the study's risks and benefits in terms of developments in the field, changing practice patterns, and new IRB policies and procedures.

To date, we have enrolled 18 subjects with Adult Separation Anxiety Disorder (13 females, 5 males). Study procedures have been generally well tolerated. One serious adverse event occurred and has been reported to the IRB, involving a patient reported to have been admitted to a hospital with the flu (and subsequently found to have been on placebo).

There have not been any study findings, recent literature, or untoward events occurring here or at other sites in the past year which might affect the analysis of the safety, risks or benefits of study participation.

Funding

Have there been any changes in funding status since the prior approval?
No
Have the principal investigator and other investigators made all required disclosures of financial interest in the study sponsor/product?
Yes

Summary

Have there been any study findings, recent literature, or untoward events occuring here or at other sites in the past year which might affect the analysis of the safety, risks or benefits of study participation?
No
Have there been any serious adverse events (serious and/or unanticipated problems involving risks to subjects or others at this site which occured in the past year)?
No
Have all study staff with a significant role in the design or implementation of the human subject components of this study received required training in human research subject protections?
Yes
Is the study covered by a certificate of confidentiality?

No

Overall Progress

Approved sample size
50
Total number of participants enrolled to date
18
Number of participants who have completed the study to date
12
Have there been any significant deviations from the anticipated study recruitment, retention or completion estimates?
Yes
Describe actions taken or planned to address these problems.
Recruitment was initially much slower than anticipated. We expanded recruitment approaches and have had a much greater flow of participants (n=13) in the past year.
Comments / additional information
None

Sample Demographics

Specify population
Adults with separation anxiety disorder
Total number of participants enrolled from this population to date
18
Gender, Racial and Ethnic Breakdown

Female patients: N = 13
Male patients: N = 5

Race:
Other: N = 3
Asian: N = 2
African American: N = 5
Caucasian: N = 8

Summary of Current Year's Enrollment and Drop-out

Number of participants who signed consent in the past year
13
Number of participants currently enrolled
4
Did the investigator withdraw participants from the study?
Yes

Circumstances of withdrawal:

One participant, missed her period, then stopped her medication. Subsequent pregnancy test was negative. She was discontinued from study due to having been off study medication for more than 5 days.

One participant was withdrawn from the study because she missed an appointment and did not respond to multiple attempts to contact her.

Did participants decide to discontinue study involvement?
Yes
Circumstances of discontinuation:
One participant asked to discontinue study involvement due to adverse events including complaints of acid taste in mouth, swollen legs, insomnia, feeling edgy, sensitivity to sound and light.

Procedures

To create the protocol summary form, first indicate if this research will include any of the following procedures

✓ Psychiatric Assessment
✓ Collection of Biological Specimens
✓ Medication Trial
✓ Medication-Free Period or Treatment Washout
✓ Off-label Use of Drug or Device

Population

Indicate which of the following populations will be included in this research

✓ Adults
✓ Adults over 50

Research Support/Funding

Will an existing internal account be used to support the project?
No
Is the project externally funded or is external funding planned?
Yes
Select the number of external sources of funding that will be applicable to this study

Funding Source #1

Is the PI of the grant/contract the same as the PI of the IRB protocol?
Yes
Select one of the following
The grant/contract is currently funded
Source of Funding
Industry
Sponsor
Forest Laboratories
Is the study investigator initiated?
Yes
Select one of the following
Single Site
Business Office
RFMH
Does the grant/contract involve a subcontract?
No

Study Location

Indicate if the research is/will be conducted at any of the following
✓ NYSPI
This protocol describes research conducted by the PI at other facilities/locations
No

Lay Summary of Proposed Research

Lay Summary of Proposed Research
Separation Anxiety Disorder is a prevalent condition that has been newly placed in the Anxiety Disorders section of DSM5. Though separation anxiety was previously assumed to be confined to childhood, the National Comorbidity Survey Replication revealed a 6.6% lifetime and 1.9% 12 month prevalence of adult separation anxiety disorder (ASAD) in the community. Symptoms of ASAD include excessive distress when facing or anticipating separation from home or from attachment figures, as well as persistent worries about permanently losing or being abandoned by attachments, or of potential harm that may befall them during separations. Individuals with ASAD may be afraid to be alone or without an attachment figure close at hand, and may avoid leaving home, sleeping in bed alone, or sleeping away from home because of separation fears. **There have been no controlled trials or established medication or psychotherapy treatments for ASAD.** Vilazodone (Viibryd) appears to have an ideal pharmacological profile for efficacy for ASAD. In well-developed animal models of separation distress, 5HT1a agonists and serotonin reuptake inhibitors (SSRIs) have shown efficacy. In children, large randomized controlled trials have reported SSRI efficacy for mixed anxiety disorders which are highly comorbid in childhood, including separation anxiety disorder, social anxiety disorder, and generalized anxiety disorder.
In this randomized clinical trial, 40 adults with a principal diagnosis of ASAD, **no major depression of**

greater than mild severity, and no substance abuse disorders will be randomized to 12 weeks of treatment with vilazodone (flexibly dosed) or matched pill placebo. Outcome will be assessed in respect to symptomatic improvement, quality of life, adverse events and safety.

Background, Significance and Rationale

Background, Significance and Rationale
Separation Anxiety Disorder is a prevalent condition that has been newly placed in the Anxiety Disorders section of DSM5. Though separation anxiety was previously assumed to be confined to childhood, the National Comorbidity Survey Replication revealed a 6.6% lifetime and 1.9% 12 month prevalence of adult separation anxiety disorder (ASAD) in the community (NCS-R, Shear et al. 2006). Symptoms of ASAD include excessive distress when facing or anticipating separation from home or from attachment figures, as well as persistent worries about permanently losing or being abandoned by attachments, or of potential harm that may befall them during separations. Individuals with ASAD may be afraid to be alone or without an attachment figure close at hand, and may avoid leaving home, sleeping in bed alone, or sleeping away from home because of separation fears. There are no established medication or psychotherapy treatments for ASAD. Vilazodone (Viibryd) appears to have an ideal pharmacological profile for efficacy for ASAD. In well-developed animal models of separation distress, 5HT1a agonists and serotonin reuptake inhibitors (SSRIs) have shown efficacy (Winslow and Insel 1991; Simpson et al. 2007). In children, large RCTs have reported SSRI efficacy for mixed anxiety disorders which are highly comorbid in childhood, including separation anxiety disorder, social anxiety disorder, and generalized anxiety disorder (Walkup et al. 2001, 2008).
In this randomized clinical trial, 40 adults with a principal diagnosis of ASAD and no major depression or substance abuse disorders will be randomized to 12 weeks of treatment with vilazodone (flexibly dosed) or matched pill placebo. Outcome will be assessed in respect to symptomatic improvement, quality of life, adverse events and safety.

Specific Aims and Hypotheses

Specific Aims and Hypotheses
Aim 1. To assess the efficacy of vilazodone in the treatment of adult separation anxiety disorder (ASAD).
Primary Hypothesis (1): ASAD patients randomized to 12 weeks of vilazodone treatment will evidence greater symptomatic improvement than those randomized to placebo.
Hypothesis 2: ASAD patients randomized to 12 weeks of vilazodone treatment will evidence greater improvement in quality of life than those randomized to placebo.

Aim 2. To assess the safety and acceptability of vilazodone in the treatment of ASAD. Data will be collected on adverse events and duration of treatment.

Description of Subject Population

Sample #1

Specify subject population
adults with separation anxiety disorder
Number of completers required to accomplish study aims
40 randomized
Projected number of subjects who will be enrolled to obtain required number of completers
50
Age range of subject population
18-60

Gender, Racial and Ethnic Breakdown
We anticipate randomizing 30 women and 10 men; 20 Hispanics and 20 non-Hispanics; 27 whites, 10 African-Americans, and 3 Asians.
Description of subject population
Men and women, of any race and ethnicity, who present for treatment of DSM5 ASAD at the Anxiety Disorders Clinic of the New York State Psychiatric Institute.

Recruitment Procedures

Describe settings where recruitment will occur
Anxiety Disorders Clinic
How and by whom will subjects be approached and/or recruited?
Subjects who respond to treatment notices will be screened on the phone by a research assistant. After psychiatric assessment, the assessing psychiatrist will invite eligible subjects to participate in the study.
How will the study be advertised/publicized?
Patients will be obtained through: (a) word-of-mouth referrals from former patients, (b) referral from area medical and mental health professionals, (c) publicity about the study, including articles in local newspapers and magazines, appearances on local radio and television shows, etc., leading to self-referral of prospective patients, (d) recruitment notices placed in local media and on the internet (i.e. Facebook and Twitter), (e) Columbia Recruit Me, (f) Radio audio ads
Do you have ads/recruitment material requiring review at this time?
Yes
Does this study involve a clinical trial?
Yes
Please provide the NCT Registration Number
NCT01999920

Concurrent Research Studies

Will subjects in this study participate in or be recruited from other studies?
Yes

Describe concurrent research involvement
From the Anxiety Disorders Clinic psychiatric screening evaluation protocol (IRB #5029)

Inclusion/Exclusion Criteria

Name the subject group/sub sample
Adult Separation Anxiety Disorder patients
Create or insert table to describe the inclusion criteria and methods to ascertain them

Inclusion criteria:	Method of Ascertainment
1. Males or females between the ages of 18 and 60	History
2. Current primary (most clinically significant) diagnosis of DSM5 ASAD	**SCID-I**, Clinical Interview for ASAD
3. Able to give consent, fluent in English.	Clinical Interview

Create or insert table to describe the exclusion criteria and methods to ascertain them

1. Past or current DSM-IV diagnosis of any psychotic disorder; organic mental disorder or other cognitive disorder; bipolar disorder; or antisocial personality disorder. Current MDD of moderate or greater severity. Any other current primary Axis I disorder.	**SCID-I,** Hamilton Depression Scale 17-item total >18
2. Recent history (past 3 months) of substance or alcohol abuse or dependence (other than nicotine or caffeine).	**SCID-I**, urine toxicology
3. Suicidal ideation or behavior (in the past year) that poses a significant danger to the subject.	Psychiatric interview, Score >2 on suicidal ideation item of Hamilton Depression Scale
4. Medical illness that could significantly increase risk of vilazodone treatment or interfere with assessment of diagnosis or treatment response, including including organic brain impairment from stroke,CNS tumor, or demyelinating disease; renal, thyroid, hematologic or hepatic impairment; diabetes mellitus.	Medical chart review, physical exam, blood and urine tests Consultation with primary care doctor when indicated.
5. Current or past history of seizure disorder (except febrile seizure in childhood	Medical history, psychiatric

	interview
6. History of non-response to ≥ 2 serotonergic reuptake inhibitor antidepressants (SSRIs and/or SNRIs) for the treatment of ASAD after adequate treatment trials (adequate treatment is defined as at least 8 weeks at an adequate dose[s] based on approved package insert recommendations).	Medical history
7. Currently taking medication which has been effective for patient's ASAD.	Psychiatric Interview
8. For patients taking any ineffective psychoactive drug or herbal remedy, inability to tolerate or unwillingness to accept a drug-free period prior to beginning the study of 2 weeks or 5 half-lives (whichever is longer) before beginning study treatment, or ever having been treated with a depot antipsychotic. Fluoxetine washout period will be at least 5 weeks.	Psychiatric Interview
9. Requiring concomitant treatment with any prohibited medications, supplements, or herbal remedies, except for zolpidem, or zolpidem extended release for insomnia, which may be continued provided the medication has been used in a consistent manner for 4 weeks prior to randomization.	Psychiatric interview
10. History of intolerance or hypersensitivity to vilazodone, SNRIs or SSRIs.	Psychiatric Interview
11. History of light therapy, electroconvulsive therapy, vagus nerve stimulation, transcranial magnetic stimulation, or any other experimental procedure for central nervous system disorders within 6 months of beginning this study.	Psychiatric Interview
12. Pregnancy, lactation; for women of childbearing potential, not using an effective birth control method (e.g. oral contraceptive or double barrier method) for the duration of the study.	History, Physcial exam, blood pregnancy test
13. Current formal psychotherapy initiated within 3 months of beginning this study. This includes: psychodynamic, cognitive-behavioral and interpersonal	History

therapies.

Waiver of Consent/Authorization

Indicate if you are requesting any of the following consent waivers
Waiver of consent for use of records that include protected health information (a HIPAA waiver of Authorization)
No
Waiver or alteration of consent
No
Waiver of documentation of consent
No
Waiver of parental consent
No

Consent Procedures

Is eligibility screening for this study conducted under a different IRB protocol?
Yes
Indicate NYSPI IRB #
5029
Describe Study Consent Procedures
The study psychiatrist will determine eligibility and fully explain study procedures. Patients interested in participating in research, who understand the risks and benefits of participation, will provide informed written consent to participate.
Patients currently taking psychotropic medication will be carefully evaluated for history of response. Patients with inadequate response (persistent diagnosis of ASAD and meeting other inclusion/exclusion criteria) to current medication will be evaluated to ascertain that they are receiving the appropriate dose of that medication. They will be asked for consent to contact their prescribing doctor. After consultation with the pre-study prescribing doctor (if patient consented to contact), patients will be brought up to the maximal appropriate dose before determining their eligibility for this study. For patients who remain inadequately responsive after an adequate trial of their current medication, after the patient consents to participate in this study, the patient will be instructed on how to taper medication as clinically indicated to minimize discontinuation-related adverse effects. A study psychiatrist will see the patient weekly during this period **and complete a CGI-change scale -- a score of 6, much worse, or greater will trigger additional clinical assessment and prompt a discussion about continued participation**. Such subjects will discontinue prohibited medication for > 2 weeks, or 5 half-lives (whichever is longer), (and 5 weeks for fluoxetine), before proceeding with the pretreatment assessment. Patients with inadequate response to vilazodone will be excluded. Patients will not be withdrawn from effective treatment for the purpose of entering this study.
Indicate which of the following are employed as a part of screening or main study consent procedures

✓ Consent Form

Persons designated to discuss and document consent

Select the names of persons designated to obtain consent/assent
Campeas, Raphael, MD
Schneier, Franklin, MD
Type in the name(s) not found in the above list

Study Procedures

Describe the procedures required for this study

Week 0 Baseline Visit. Randomization and Pretreatment Assessment Subjects will be randomized to vilazodone or placebo by a computer-generated random-number program, with treatment assignment sealed in opaque envelopes. Randomization sequences will be provided by the study statistician, who has no contact with study subjects.

Treatments. Subjects will initially receive 12 weeks of treatment with a single psychiatrist. The baseline treatment visit will last 45 minutes and subsequent visits 30 minutes. The first session will serve the following purposes: (1) confirm history; (2) obtain baseline ASAD symptoms; (3) provide explanatory framework for treatment; (4) address issues/concerns about medication; (5) describe specific side effects and characteristic medication response patterns; (6) establish a warm, empathic relationship, and engage the patient's trust; (7) explain the purpose and design of the study; and (8) make clear to the patient that the physician recognizes, understands and is familiar with ASAD. To ensure external validity, treating psychiatrists do not provide instructions about any exposure or cognitive therapy exercises. At the end of each visit pills will be provided as vilazodone 10 or 20 mg pills (depending on total dose), and matching placebo. A sufficient supply will be provided to last until the next visit (+/-3days), and unused medication will be collected from the patient at each visit. Brief ratings will be conducted by the psychiatrist to assess depression and adverse events, and vital signs will be assessed.
Dosage will initially be prescribed according to a fixed schedule, which may be modified in the case of nonresponse or intolerable side effects. It will start at 10mg/day and be increased to 20mg/day after 1 week and 40 mg/day after two weeks (optional). Patients without significant adverse effects who are not remitted (CGI-I=1) will have their dose increased to a maximum of 40 mg/day for the remainder of the study, if tolerated. Dosage can be held steady or lowered at any time during the study as clinically indicated in the event of adverse effects.
At the week visit 12 (or at premature termination), a complete medical workup (bloods, urine, EKG, physical exam) will be repeated. Participants at week 12 will be offered post-study open treatment and referrals, including the option of continuing on vilazodone if clinically appropriate. If discontinuation of study vilazodone is clinically indicated at any time, dosage will be tapered according to the following schedule, based on dose at endpoint:

Endpoint Dose	Taper Schedule
40mg	-->20mg for 4 days, 10mg for 7 days, then discontinue.

30mg -->20mg for 4 days, 10 mg for 7 days, then discontinue
20mg -->10 mg for 7 days, then discontinue.
10mg --> discontinue

Subjects will also complete a computer-based Attention Bias Measurement at baseline, week 1, and week 12 visits, using procedures developed by Bar Haim (2010). This will assess bias to look toward angry or neutral faces, as a predictor and correlate of treatment response.

The stimuli are face photographs of 20 different individuals, with an angry and a neutral expression for each individual. The protocol consists of 120 trials (80 angry-neutral and 40 neutral-neutral presentations). Each trial begins with a fixation cross "+" presented in the center of the monitor for 500 ms. Immediately following termination of the fixation cue, the computer presents two faces of the same individual, positioned vertically. Each pair of faces displays one of two combinations of emotions (i.e., neutral and angry, or neutral and neutral).

After presentation of the face pair for 500 ms, a probe ("<" or ">") appears in the location of one of the faces. Participants are instructed to press the button (left or right, corresponding to the direction of the probe pointer).

The task takes 5-10 minutes to complete.

You can upload charts or diagrams if any

Criteria for Early Discontinuation

Criteria for Early Discontinuation
Adherence and termination of study treatments
Adherence -- Rules of the treatment protocol will be carefully explained to patients by intake screeners and in consent forms. Patients who miss study visits will be actively followed up by phone and mail. Serious protocol violations, such as use of proscribed outside treatments or substance abuse, will be reviewed by the PI and will result in withdrawal from the study treatment. Substance use will be assessed by initial drug screen and subsequent patient report. If clinical suspicion of substance use arises based on erratic behavior, alcohol on breath, and other signs and symptoms, spot toxicology screens will be used. Treating psychiatrists will monitor patient drinking behavior with repeated queries over the course of treatment. If patients are withdrawn from the study treatments, staff will make every effort to make this event constructive and empathic. Patients will continue to be assessed for the full **12** weeks of the study. A pill count will be conducted after each visit to assess adherence to medication schedule.
Criteria for removal from study treatment, including non-adherence. These will be defined as follows: a) patients who deteriorate in treatment, as defined during weeks 0-12 by CGI-I score > 5 and remain similarly impaired at re-assessment one week later; b) patients who commit serious violations of the protocol; and c)

patients who miss more than 3 consecutive days of medication or a total of 12 days within weeks 0-12. Patients who are non-adherent with a clinic visit will be contacted by the investigator to elucidate reasons for non-adherence.

Blood and other Biological Samples

Please create or insert a table describing the proposed collection of blood or other biological specimens

Prior to study entry, and at the week 12 visit, **25ml** of blood will be drawn for: **oxytocin levels**, CBC, chemistry, thyroid tests, and in women, pregnancy test. Urine will be obtained for drug screen and urinalysis.

Assessment Instruments

Create a table or give a brief description of the instruments that will be used for assessment
(1 hour) Structured Clinical Interview for DSM IV (SCID-I) (First et al., 2002), used to determine Axis I disorders
(10 min) Structured Clinical Interview for Separation Anxiety Disorder (Cyranowski et al., 2002), modified for DSM-5. The eight separation anxiety disorder criteria are rated for both childhood (rated at baseline only) and past week time frames, scored as 0 (not at all), 1 (sometimes), 2 (often) or ? (don't recall). In keeping with the DSM-5 guidelines, endorsement of three or more of the eight criterion symptoms (symptoms rated as '2' or 'often') is used as a threshold to determine categorical (yes/no) diagnosis of separation anxiety disorder. Scores on each of the eight items are also summed to produce a continuous measure of separation anxiety symptoms experienced during childhood and adulthood (range for each scale=0–16).
(10 min) Hamilton Rating Scale for Depression (Hamilton, 1960) This standard scale will be used to assess severity of depression.
(10 min) Quality of Life Enjoyment & Satisfaction Questionnaire (Q-LES-Q, Endicott et al, 1993): self-rated assessment of quality of life.
(5 min) Arizona Sexual Experiences Scale (ASEX) (McGahuey et al., 2000): will be used to assess sexual functioning as a self-rating. It is a five-time rating scale and has been shown to have adequate internal consistency, test-retest reliability, and convergent and discriminant validity.
(5 min) Anxiety Sensitivity Index (Peterson and Reiss 1993): self-rated and measures anxiety sensitivity or fear of anxiety-related sensations
(1 min) Sheehan Disability Scale (Sheehan 1983): self-rated and assesses functional impairment in work/school, social life, and family life.
(10 min) Hamilton Anxiety Scale (Hamilton 1959): measures the severity of both psychic and somatic anxiety.
(5 min) Clinical Global Impression-Improvement Scale (CGI-I), a quickly administered and widely used observer rating, will evaluate overall clinical status on a 1-7 point likert scale (Guy, 1976).
(5 min) Side Effect Checklist (SECL) A checklist of 27 symptoms commonly occurring as side effects to SSRIs will be rated on a 4-point anchored scale from 0-none to 3-severe.

(15 min) Adult Separation Anxiety – 27 Scale (Manicavasagar et al, 2003) 27 items pertaining to adult separation anxiety, each self-rated on a four-point scale.
(15 min) Attachment Style Questionnaire (Feeney at al., 1994) 40 items relating to quality of adult relationships, each self-rated on a four-point scale.

Please attach copies, unless standard instruments are used

Off label and investigational use of drugs/devices

Choose from the following that will be applicable to your study
✓ Drug
Select the number of drugs used in this study
1

Drug #1

Name of the drug
Vilazodone
Manufacturer and other information

Forest Laboratories

Vilazodone is an SSRI and 5HT1a receptor agonist, FDA-approved for depression.

Approval Status
No IND is required
Choose one of the following options
FDA has determined that IND is not required

Research Related Delay to Treatment

Will research procedures result in a delay to treatment?
Yes
Maximum duration of delay to any treatment

Maximum duration of delay to any treatment would be one week for assessments, except that patients who are to be tapered off ineffective medication will have an additional delay of 2-4 weeks for washout, plus the time needed to taper off.

Patients randomized to placebo could have active treatment delayed by another 12 weeks (maximum total of 17 weeks including assessment and washout, if needed).
Maximum duration of delay to standard care or treatment of known efficacy

The is no treatment of known efficacy for ASAD, as there have been no reported clinical trials of medication of psychotherapy for this condition. However, based on studies of separation anxiety disorder in children, standard care might consist of cognitive-behavioral therapy or SSRI medication. The maximum duration of delay to standard care would be 17 weeks, as described above for subjects who needed a 5-week washout, and were then randomized to placebo.

Treatment to be provided at the end of the study
Three months of open medication treatment, including one month of free medication.

Clinical Treatment Alternatives

Clinical treatment alternatives
Based on studies of childhood separation anxiety disorder, the main treatment alternatives are cognitive-behavioral therapy or SSRI medication.

Risks/Discomforts/Inconveniences

Risks that could be encountered during the study period

a. Risks Associated with Treatment Procedures:
Medication Treatment: The most commonly reported side effects associated with therapeutic doses of vilazodone (incidence ≥ 5% and at least twice the rate of placebo) are: diarrhea, nausea, vomiting, and insomnia. Uncommon potential side effects include serotonin syndrome, increased bleeding, mania and low blood sodium. Suicidal ideation has been reported to sometimes be associated with antidepressant treatment. Vilazodone may have negative interactions with other medications a patient may take over the course of the study.

Medication Discontinuation: Tapering of vilazodone that is too abrupt may lead to symptoms such as dizziness, sensory disturbances, agitation or anxiety, nausea and sweating. For patients who are tapered off study medication by study psychiatrists for any reason, tapering will be gradual and closely monitored.

Prohibited Treatments: An additional risk is that participants will not be able to benefit from all available treatments, as they will be prohibited from receiving other potentially helpful treatments during the study, including other psychotropic medications or initiating psychotherapy.

Placebo: Patients have a 50% chance of being assigned to placebo for the 12 weeks. These participants will not be receiving active pharmacological treatment, and their condition could fail to improve or could worsen during this period.

Blind Treatment: Another risk is that participants will not be told whether they were assigned to vilazodone or placebo until completing the 14 week assessment period, except in the event of a medical emergency. This may delay or interfere with selection of optimal post-study treatments.

b. Risks Associated with Assessment Procedures:
Venipuncture: Mild discomfort and, rarely, a small arm bruise, clot or infection may occur at the site of the blood drawing.

Self-Report Measures, Assessor Ratings: Patients could develop mild to moderate emotional discomfort or frustration associated with psychiatric interviewing or filling out questionnaires.
Describe procedures for minimizing risks

To minimize treatment risks, patients will be screened for conditions that significantly increase risks of treatment, adverse effects and vital signs will be monitored at every visit, and dosing is flexible to allow reductions in the event of adverse effects. Patients will be educated about potential adverse interactions with other medications they may wish to take and advised to contact study physicians before starting new medications. Patients will be informed that they may withdraw from study treatment at any time. Randomization codes will be broken for patients upon their termination from the study, or earlier in the event of a medical emergency.

Venipuncture will be conducted with standard safety procedures.

Self-Report Measures, Assessor Ratings: Study clinicians are skilled at dealing with distress and will make efforts to help clients to feel as comfortable as possible (e.g., by giving breaks during an evaluation, offering encouragement).

Methods to Protect Confidentiality

Describe methods to protect confidentiality
All data with identifying information will be stored in locked file cabinets or password-protected computer files. Data being analyzed will be identified by subject codes and identifying information will be removed. The identity of patients will not be revealed in the presentation or publication of any results from the project. All assistants and others working on the project will be educated about the importance of strictly respecting patients' rights to confidentiality.
Will the study be conducted under a certificate of confidentiality?
No

Direct Benefits to Subjects

Direct Benefits to Subjects
The potential direct benefit to patients who enter this study will be to obtain relief from ASAD symptoms to improve their quality of life. Vilazodone is an SSRI, and SSRIs have appeared efficacious for childhood separation anxiety disorder. Also, Vilazodone is FDA-approved for the treatment of depression, and it may be helpful for comorbid symptoms of depression in ASAD.

Compensation and/or Reimbursement

Will compensation or reimbursement for expenses be offered to subjects?
Yes
Please describe and indicate total amount and schedule of payment(s).
Include justification for compensation amounts and indicate if there are bonus payments.
Participants will receive $30/evaluation for completing each visit 2,3,4,5,6, and 7; $60/evaluation for completing each visit 1 and 8, to be paid by cash after each visit (maximum total of $300 over the 12 weeks of the study).

Subjects will be paid for each of these assessments that are completed at the specified week, regardless of whether they are continuing on study treatment or not.

Uploads

Upload the entire grant application(s)
Upload copy(ies) of unbolded Consent Form(s)
CF unbolded 9.30.16.pdf
Upload copy(ies) of bolded Consent Form(s)
CF bolded 9.30.16.pdf
Upload copy(ies) of recruitment materials/ads to be reviewed
ads sep anxiety revision 1.pdf
ASAD ad 9.6.16.pdf
Sep_Anx_Ad_pull_tabs.pdf
Sep_Anx_Ad_loved_one.pdf
Vilaz_Paid_Craigslist_Posting_.pdf
Sep Anx Ad partner or spouse (no stamp).pdf
Sep Anx Ad child (no stamp).pdf
Upload copy(ies) of the HIPAA form
HIPAA_09.06.16.pdf
Upload any additional documents that may be related to this study
Continuation_memo.approved_pending.09.30.16.pdf

References

References

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Relationship Anxiety Study

Are you anxious about relationships?
Worry about being separated from someone you care about?
Find it hard to travel or sleep apart from someone you are close to?
Worry about harm to people you are close to?
Avoid being alone?
Concerned you may be too clingy?
Are these symptoms interfering with your life?

If you are age 18-60, you may be eligible to participate in a ***research*** study of medication for treatment of an anxiety disorder. Eligible persons will receive payment for their participation. For more information please contact Rob at (646) 774-8113 or valdovi@nyspi.columbia.edu. All calls are strictly confidential.

***Free Evaluation**

Anxiety Disorders Clinic
New York State Psychiatric Institute/RFMH

(646) 774-8113 Separation Anxiety Study	(646) 774-8113 Separation Anxiety Study	(646) 774-8113 Separation Anxiety Study	(646) 774-8113 Separation Anxiety Study	(646) 774-8113 Separation Anxiety Study	(646) 774-8113 Separation Anxiety Study	(646) 774-8113 Separation Anxiety Study	(646) 774-8113 Separation Anxiety Study	(646) 774-8113 Separation Anxiety Study	(646) 774-8113 Separation Anxiety Study	(646) 774-8113 Separation Anxiety Study	(646) 774-8113 Separation Anxiety Study	(646) 774-8113 Separation Anxiety Study

Do You Have Separation Anxiety?

Do you constantly worry about your loved ones?
Concerned about being separated from someone you care about?
Experience excessive stress when anticipating separation from attachment figures or home?
Find it hard to travel or sleep apart from those you are close to?
Worry about harm to people you are close to?
Avoid being alone?
Concerned you may be too clingy?
Are these symptoms interfering with your life?

If you are between the ages of 18-60 and are suffering from some of these conditions, you may be eligible to participate in a ***paid research study*** of medication for treatment of separation anxiety disorder. Eligible persons will receive payment for their participation. Please call for more information. All calls are strictly confidential.

***Free Evaluation**

Anxiety Disorders Clinic
New York State Psychiatric Institute/RFMH
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dmoskow@nyspi.columbia.edu

Do You Have Separation Anxiety?

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If you are between the ages of 18-60 and are suffering from some of these conditions, you may be eligible to participate in a ***paid research*** study of medication for treatment of Separation Anxiety Disorder in adults. Eligible persons will receive payment for their participation. For more information please contact Danielle at (646) 774-8113 or dmoskow@nyspi.columbia.edu. All calls are strictly confidential.

***Free Evaluation**

Anxiety Disorders Clinic
New York State Psychiatric Institute/RFMH

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CONSENT FORM – Cover Sheet

Vilazodone for Separation Anxiety Disorder in Adults Overview of Study

Purpose: To compare the effectiveness of the antidepressant medicine vilazodone, versus placebo, in the treatment of Separation Anxiety Disorder in adults. There have been no published studies of the treatment of Separation Anxiety Disorder in adults.

Procedures:

- Eight visits to the Anxiety Disorders Clinic over a 12-week period Research treatment for 12 weeks:
  - Half of participants will be assigned to take vilazodone (Viibryd), a treatment that is FDA-approved for depression, but has not been previously studied for separation anxiety disorder.
  - Half of participants will be assigned to take a placebo (inactive pill).
  - Assignment to vilazodone or placebo will be done at random (flip of a coin), and you will not find out which you are getting until you end study participation.
  - You will be asked to not start psychotherapy during the time of your participation in this study.

Risks:

- Study medication may not help.
- Side effects may occur.
- Pregnant women should not participate in this study.

Compensation: Up to $300 total for completing all study visits.

Confidentiality: All records will be confidential to the extent permitted by law.

Your Rights: Your participation is voluntary, and you may withdraw from the study at any time and seek alternative treatment if you wish.

CONSENT FORM

Vilazodone for Separation Anxiety Disorder in Adults

Contact for questions and emergencies

Dr. Franklin Schneier or your study doctor is available to answer your questions at any time. They can be reached during the day at (646) 774-7000. After 5 PM you can page the
Anxiety Clinic Doctor on Call at (917) 996-6939. Dr. Schneier can be reached by mail at Unit 69, 1051 Riverside Drive, New York, NY 10032.

PURPOSE OF STUDY

You are being asked to participate in this research study because you are an adult with Separation Anxiety Disorder. This study compares the effectiveness of vilazodone (brand name Viibryd) to placebo in the treatment of 40 persons with Separation Anxiety Disorder. The placebo looks like the other pill, but does not contain any medicine (it is sometimes called a “sugar pill”). There are no published studies of treatments for adults with Separation Anxiety Disorder and no medications approved for this condition. Vilazodone is a medication that is FDA-approved for the treatment of depression but has not been studied for Separation Anxiety Disorder. This study is sponsored by Forest Laboratories, the manufacturer of vilazodone.

ALTERNATIVE TREATMENTS

You do not have to participate in this study to receive treatment for Separation Anxiety Disorder. Vilazodone is available by prescription and can be prescribed by your regular medical doctor. Other treatments for Separation Anxiety Disorder include psychotherapy such as cognitive behavioral therapy, and off-label use of antidepressants, such as

paroxetine (brand name Paxil) or sertraline (brand name Zoloft). Your doctor will discuss benefits, risks and side effects of study participation with you. The alternative to participating in this study would be to get treatment elsewhere without the research interviews and procedures, and without the possibility of getting a placebo.

STUDY PROCEDURES

This study involves your taking study pills daily, and visiting the Anxiety Disorders Clinic up to 8 times (total of 4-1/2 hours) over 12 weeks. You will be assigned at random (flip of a coin, with a 50/50 chance for each) to take either vilazodone or placebo. Neither you nor the researchers will know if you are getting the placebo (inactive pill), but they can find out in an emergency.

You have already met with your study doctor to discuss your medical and psychiatric condition. In addition, you were asked standard questions and received a medical exam, including blood and urine tests, a urine drug screen and an electrocardiogram (EKG).

You will need to be off all psychiatric medication for at least two weeks before starting study treatment, except for the sleep medication zolpidem (brand name Ambien or Ambin CR). If you have been taking zolpidem consistently over the four weeks prior to study treatment, you will be allowed to continue using it during the study. During the study you should not take any medication nor receive any psychotherapy without approval of your study doctor.

If you are taking a medication that has been helpful but is not allowed in the study, you cannot participate in the study. If you are on medication that has not been helpful and is not allowed in the study, your study doctor will ask your permission to contact your treating doctor. If you agree, the medication will be stopped in consultation with your treating doctor. You will be monitored with weekly visits during this period. If you are on medication that has not been helpful and you do not want your treating doctor to be contacted, you will not be able to participate in this study.

To participate in this study, you must agree to avoid using alcoholic beverages or recreational drugs during the study, because they might cause problems if combined with your medication. You must also agree to avoid starting psychotherapy during the study, because it could interfere with evaluating the study medications.

Study Treatment

You will see your study doctor for about 30 minutes weekly for two weeks, and then every other week for six weeks, and then four weeks later. At each visit your study doctor will ask about any improvements or side effects that you have noticed. The doctor will adjust the dose of the medicine to try to maximize your improvement. The doctor will give you study medication (vilazodone or placebo), which you should take as instructed. The medication should not be taken by anyone else, and it should be kept in a safe place out of the reach of children.

You will also be asked about your symptoms by a study rater at each visit. You will also be asked to complete questionnaires at each visit. At three of the study visits, you will also be asked to sit at a computer monitor for about 10 minutes and view pictures of faces and then a pointer ("<" or ">"). You will be asked to press a left or right button, depending on the direction of the pointer.

After 12 weeks of treatment, you will complete the same medical exam you received at the beginning of treatment (physical exam, blood tests [equivalent of two tablespoons], urine tests, EKG). If you are discontinuing study medication you will be given instructions on how to reduce it gradually.

The doctor in charge of the study can remove you from the study without your consent for one of the following reasons:

- If in his judgment, you need an alternative treatment.
- If you fail to follow the study rules.
- If your condition significantly worsens during the study.

Treatment After You End Study Treatment

At the time you end study treatment you will be offered further treatment in the clinic with vilazodone or with another medication if recommended by your clinic doctor, for three months. All visits with your doctor will be free of charge for three months. Medication will be free of charge for the first month, and after that you may have to pay for your medication. After three months you will be referred for follow-up care if needed. If at any time after you end study treatment you would like treatment other than medication you can be referred to such treatment. You can get such treatment while you are receiving the three months of after-study medication treatment offered in the clinic.

When you leave the study, an Anxiety Disorders Clinic doctor will meet with you, inform you whether you were taking vilazodone or placebo during the study, and answer any questions you may have about this.

RISKS

Study Treatments: The main risk of this study is that the research treatments may not help your symptoms. Even if you receive vilazodone, it may not help your Separation Anxiety Disorder, and your symptoms may get worse. A common treatment for Separation Anxiety Disorder includes psychotherapy such as cognitive-behavioral therapy, but it may be up to 17 weeks from the time you enter the study until you would be provided with psychotherapy or another type of treatment, such as other medications. Additionally, because you will not find out whether you have been taking vilazodone or placebo until you leave the study (except in the event of an emergency), decisions about your treatment during the study will not be able to take that information into account.

Other possible risks to you are the side effects that some people get from vilazodone. You should not drive or operate complex or heavy machinery if study medication is affecting your thinking or reflexes. Side effects that may occur include sweating, rash, nausea, vomiting, increased or decreased appetite, weight loss or gain, sleepiness, fatigue, insomnia, dizziness, nervousness, cough, running nose, dry mouth, muscular tremors, changes in heart rate, elevated mood, and sexual problems, including

loss of interest for both sexes, difficulty having orgasm in women, and difficulty having an erection or ejaculating in men. Vilazodone may cause unexpected problems if combined with other medications you might take during the study.

Stopping vilazodone too rapidly may cause dizziness, agitation or anxiety, nausea and sweating. These symptoms usually resolve over time. You should not stop study medication before discussing it with your study doctor.

While vilazodone is considered to be a safe treatment, the Food and Drug Administration (FDA) has issued a public health advisory about a possible link, in rare cases, between suicidal thoughts or behavior in patients treated with antidepressant medications (including vilazodone). The FDA has asked health care providers and patients to note that worsening of depression could be related to the underlying disease process, or in some cases, might be a direct result of antidepressant drug treatment. At the present time, the FDA has not concluded that these drugs cause worsening depressive symptoms or suicidal ideation or behavior, and this is an area of active research. The FDA advisory urges careful monitoring of patients receiving these medications during the beginning stage of therapy and during increases or decreases in dosage.

To minimize risks of study treatment, you have been checked for conditions that can increase risks of treatment, and you will be closely monitored for side effects at every visit. A study doctor will be available by pager 24 hours/day. Your study doctor can adjust the doses of study medications to minimize side effects. If you need to take any other medications during the study, you should first contact your study doctor to minimize the risk of drug interactions. You may leave the study at any time. In the event of a medical emergency, your doctor will be able to find out what medication you have been taking during the study.

For women: **You should not be in this study if you are pregnant.** Women who take vilazodone during pregnancy or who become pregnant while taking it may be at greater risk of having a baby born with a birth defect. You must agree to use birth control

throughout the course of your treatment with medication. If you decide to stop using birth control, or if there is a possibility that you are pregnant during the study, you must tell your study doctor immediately so that a pregnancy test can be done, and we can decide whether you should continue in the study.

Blood Drawing may cause mild discomfort and, rarely, a small arm bruise, clot or infection may occur at the site.
Ratings: You may feel mild to moderate upset or frustration due to answering questions about your life or filling out questionnaires. Study staff are skilled at dealing with these events and will try to help you feel as comfortable as possible (e.g., by giving breaks during an evaluation, offering encouragement).

BENEFITS:

A direct benefit to you is the possibility that the research treatment **may** help your Separation Anxiety Disorder symptoms. In addition, your participation may help researchers learn more about how to treat Separation Anxiety Disorder. There may be no benefit to you if the treatment is not effective.

COMPENSATION:

You will receive $60 for each of the first and last visits, and $30 for each of the **6** interim visits you complete, to be paid in cash after the completion of each visit (up to $300 total), as payment for your time. You will be paid for each of these visits that you complete on schedule, whether or not you are continuing on study treatment.

CONFIDENTIALITY:

All records related to the study are confidential, although state and federal agency, and Forest Laboratories personnel may inspect records. Similarly, there are legal advocacy organizations that have the authority under the law to access otherwise confidential

subject records. They cannot re-disclose this information without the subject's consent. All records will be confidential to the extent permitted by law. Your records will be kept in locked files and access will be allowed only to members of the research team, or institutional personnel as part of a routine audit. Should any of the information gathered from you be used for scientific publications or presentations, you will be protected through the use of a system of codes that will not reveal the identity of individuals. Any report based on this study will only be used as grouped information without mention or description of the individual participants.

Your name and other personal identifying information will be stored in an electronically secure database at New York State Psychiatric Institute. Research data that is entered into the computer will be stored according to study ID number. A master list linking the patient name to the assigned ID number is kept in a separate file. To access the computer and appropriate data files, the staff member must have knowledge of the password and be given rights to access the data by the data manager. All data that is transmitted via computer is encoded and identifying information is removed.

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.

RESEARCH STANDARDS AND PARTICIPANTS' RIGHTS:

Participation in this research study is voluntary. If you decide not to participate, or if you later decide to stop participating, you will not lose any benefits to which you are otherwise entitled. A decision not to participate will not effect your treatment at the New York Psychiatric Institute. The doctors participating in this research study are also responsible for your clinical care in the Anxiety Disorders Clinic, even after you end the study. You will be notified of significant new findings that may relate to your willingness to continue to participate in the study.

Medical Compensation for Research-Related Injuries

Federal regulations require that you be informed about the institution's policy with regard to compensation and payment for treatment of research-related injuries. Short term emergency medical treatment, which has been determined to be necessary by New York State Psychiatric Institute's doctors, and which is within the capability of New York State Psychiatric Institute will be provided. In addition, you will be provided assistance in arranging follow up care in such instances.

New York State Psychiatric Institute and Research Foundation for Mental Hygiene do not provide compensation or payment for treatment of research related injuries. However, you should be aware that participation in this research does not waive any of your legal rights to seek such compensation through the courts.

Dr. Schneier or your study doctor is available to answer your questions about the study at any time. They can be reached during the day at (646) 774-7000. After 5 PM you can page the Anxiety Clinic Doctor on Call at (917) 996-6939. In addition, an emergency psychiatric consultation is always available to you by calling these numbers. The doctors participating in this research study are also responsible for your clinical care. If you have any questions about your rights as a research participant or any complaints, you may call the NYSPI-IRB Main Office at (646) 774-7155 during regular office hours.

You will be given a copy of the signed Consent Form to keep.

STATEMENT OF CONSENT

I voluntarily agree to participate in the research study described above.

NAME_____(print)

Date_____ Signature _____

Study Participant

I have discussed the proposed research with the patient, and in my opinion, this patient understands the benefits, risks and alternatives (including non-participation) and is capable of freely consenting to participate in this research.

NAME_____(print)

Date _____Signature_____

Study Physician

INSTITUTIONAL REVIEW BOARD

NEW YORK STATE PSYCHIATRIC INSTITUTE

MEMORANDUM

September 30, 2016

TO: Dr. Franklin Schneier

FROM: Dr. Edward Nunes, IRB Co-Chair

SUBJECT: Protocol #6856: VILAZODONE FOR SEPARATION ANXIETY DISORDER IN ADULTS

The Full Board reviewed the above protocol continuation application on September 26, 2016 and recommended approval pending your response to the following items. Please submit (through PRISM) **(1) a copy of this memo, (2) your point-by-point response (question and answer format), (3) the revised Protocol Summary Form (PSF) with revisions bolded, (4) the Consent Forms (CF).**

1. Please remove from the Questions section of the CF, "The NYSPI IRB has approved recruitment for this study." This is no longer approved template language.
2. Please revise the IRB contact information in the Questions section of the CF:
   *You may call the **IRB Main Office** at (646)774-**7155** during regular office hours*.

EN/alw

Adult Separation Anxiety Study

Is someone you love:

- Too clingy?
- Overly anxious when separated from you?
- Constantly contacting you?
- Worrying a lot about harm coming to you?
- Overprotective?
- Afraid to be alone or travel alone?

Do these symptoms cause problems in his or her life?

Individuals ages 18-60 who have some of these symptoms may be eligible to participate in a ***paid research study*** of medication for treatment of Separation Anxiety Disorder in adults. Eligible persons will receive payment for their participation. For more information please contact Danielle at (646) 774-8113 or dmoskow@nyspi.columbia.edu to arrange a free evaluation. All calls are strictly confidential.

Anxiety Disorders Clinic
New York State Psychiatric Institute/RFMH

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Vilazodone for Separation Anxiety in Adults (IRB# 6856)
Please note that this is an opportunity to participate in research for compensation and is not a job posting.

Do you worry too much when separated from loved ones?

We are looking for individuals with adult separation anxiety disorder (ASAD) to participate in a research treatment study. People with ASAD worry about people close to them coming to serious harm and may imagine the worst when they are apart.

This study aims to establish effective treatments for ASAD, based on what is known about the causes of separation anxiety and about treatments known to help related conditions. All information will be kept strictly confidential.

WHO CAN PARTICIPATE:

- People between the ages of 18 and 60 suffering primarily from adult separation anxiety disorder, who are not on any psychiatric medications, and who are able to travel to the New York State Psychiatric Institute/Columbia University Medical Center (1051 Riverside Drive) in Manhattan

COMPENSATION FOR PARTICIPATION:

- Total of $300, paid in installments at the end of each visit to our clinic (8 visits, total)

PROCEDURES:

1) Screening by phone (time estimate: 25 minutes)
2) If potentially eligible, an in-person psychiatric evaluation, clinical assessment, and standard health assessment (time estimate: 2 hours)
3) If eligible, 7 treatment visits to our clinic over a 12-week period (time estimate: 30-45 minutes each visit)

This is not a part-time job. Compensation is being provided for participation in a research study.

FOR MORE INFORMATION, PLEASE CONTACT:
Anxiety Disorders Clinic, Columbia University Medical Center
(646) 774-8113 or e-mail valdovi@nyspi.columbia.edu

Adult Separation Anxiety Study

Are you anxious when separated from your partner or spouse?
Are you constantly contacting your partner or spouse?
Worry a lot about harm coming to your partner or spouse?
Do you worry excessively when your partner or spouse travels?
Does your partner or spouse say you are overprotective?
Avoid activities that involve separation from your partner or spouse?
Fear being alone?
Are these symptoms interfering with your life?

If you are age 18-60, you may be eligible to participate in a ***research*** study of medication for treatment of Separation Anxiety Disorder in adults. Eligible persons will receive payment for their participation. For more information please contact Rob at (646) 774-8113 or valdovi@nyspi.columbia.edu. All calls are strictly confidential.

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09/30/2016
IRB # 6856
Sponsor: Forest Laboratories
Principal Investigator: Franklin Schneier, M.D

CONSENT FORM – Cover Sheet

Vilazodone for Separation Anxiety Disorder in Adults Overview of Study

Purpose: To compare the effectiveness of the antidepressant medicine vilazodone, versus placebo, in the treatment of Separation Anxiety Disorder in adults. There have been no published studies of the treatment of Separation Anxiety Disorder in adults.

Procedures:

- Eight visits to the Anxiety Disorders Clinic over a 12-week period Research treatment for 12 weeks:
  - Half of participants will be assigned to take vilazodone (Viibryd), a treatment that is FDA-approved for depression, but has not been previously studied for separation anxiety disorder.
  - Half of participants will be assigned to take a placebo (inactive pill).
  - Assignment to vilazodone or placebo will be done at random (flip of a coin), and you will not find out which you are getting until you end study participation.
  - You will be asked to not start psychotherapy during the time of your participation in this study.

Risks:

- Study medication may not help.
- Side effects may occur.
- Pregnant women should not participate in this study.

Compensation: Up to $300 total for completing all study visits.

Confidentiality: All records will be confidential to the extent permitted by law.

Your Rights: Your participation is voluntary, and you may withdraw from the study at any time and seek alternative treatment if you wish.

CONSENT FORM

Vilazodone for Separation Anxiety Disorder in Adults

Contact for questions and emergencies

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Anxiety Clinic Doctor on Call at (917) 996-6939. Dr. Schneier can be reached by mail at Unit 69, 1051 Riverside Drive, New York, NY 10032.

PURPOSE OF STUDY

You are being asked to participate in this research study because you are an adult with Separation Anxiety Disorder. This study compares the effectiveness of vilazodone (brand name Viibryd) to placebo in the treatment of 40 persons with Separation Anxiety Disorder. The placebo looks like the other pill, but does not contain any medicine (it is sometimes called a “sugar pill”). There are no published studies of treatments for adults with Separation Anxiety Disorder and no medications approved for this condition. Vilazodone is a medication that is FDA-approved for the treatment of depression but has not been studied for Separation Anxiety Disorder. This study is sponsored by Forest Laboratories, the manufacturer of vilazodone.

ALTERNATIVE TREATMENTS

You do not have to participate in this study to receive treatment for Separation Anxiety Disorder. Vilazodone is available by prescription and can be prescribed by your regular medical doctor. Other treatments for Separation Anxiety Disorder include psychotherapy such as cognitive behavioral therapy, and off-label use of antidepressants, such as

paroxetine (brand name Paxil) or sertraline (brand name Zoloft). Your doctor will discuss benefits, risks and side effects of study participation with you. The alternative to participating in this study would be to get treatment elsewhere without the research interviews and procedures, and without the possibility of getting a placebo.

STUDY PROCEDURES

This study involves your taking study pills daily, and visiting the Anxiety Disorders Clinic up to 8 times (total of 4-1/2 hours) over 12 weeks. You will be assigned at random (flip of a coin, with a 50/50 chance for each) to take either vilazodone or placebo. Neither you nor the researchers will know if you are getting the placebo (inactive pill), but they can find out in an emergency.

You have already met with your study doctor to discuss your medical and psychiatric condition. In addition, you were asked standard questions and received a medical exam, including blood and urine tests, a urine drug screen and an electrocardiogram (EKG).

You will need to be off all psychiatric medication for at least two weeks before starting study treatment, except for the sleep medication zolpidem (brand name Ambien or Ambin CR). If you have been taking zolpidem consistently over the four weeks prior to study treatment, you will be allowed to continue using it during the study. During the study you should not take any medication nor receive any psychotherapy without approval of your study doctor.

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Study Treatment

You will see your study doctor for about 30 minutes weekly for two weeks, and then every other week for six weeks, and then four weeks later. At each visit your study doctor will ask about any improvements or side effects that you have noticed. The doctor will adjust the dose of the medicine to try to maximize your improvement. The doctor will give you study medication (vilazodone or placebo), which you should take as instructed. The medication should not be taken by anyone else, and it should be kept in a safe place out of the reach of children.

You will also be asked about your symptoms by a study rater at each visit. You will also be asked to complete questionnaires at each visit. At three of the study visits, you will also be asked to sit at a computer monitor for about 10 minutes and view pictures of faces and then a pointer ("<" or ">"). You will be asked to press a left or right button, depending on the direction of the pointer.

After 12 weeks of treatment, you will complete the same medical exam you received at the beginning of treatment (physical exam, blood tests [equivalent of two tablespoons], urine tests, EKG). If you are discontinuing study medication you will be given instructions on how to reduce it gradually.

The doctor in charge of the study can remove you from the study without your consent for one of the following reasons:

- If in his judgment, you need an alternative treatment.
- If you fail to follow the study rules.
- If your condition significantly worsens during the study.

Treatment After You End Study Treatment

At the time you end study treatment you will be offered further treatment in the clinic with vilazodone or with another medication if recommended by your clinic doctor, for three months. All visits with your doctor will be free of charge for three months. Medication will be free of charge for the first month, and after that you may have to pay for your medication. After three months you will be referred for follow-up care if needed. If at any time after you end study treatment you would like treatment other than medication you can be referred to such treatment. You can get such treatment while you are receiving the three months of after-study medication treatment offered in the clinic.

When you leave the study, an Anxiety Disorders Clinic doctor will meet with you, inform you whether you were taking vilazodone or placebo during the study, and answer any questions you may have about this.

RISKS

Study Treatments: The main risk of this study is that the research treatments may not help your symptoms. Even if you receive vilazodone, it may not help your Separation Anxiety Disorder, and your symptoms may get worse. A common treatment for Separation Anxiety Disorder includes psychotherapy such as cognitive-behavioral therapy, but it may be up to 17 weeks from the time you enter the study until you would be provided with psychotherapy or another type of treatment, such as other medications. Additionally, because you will not find out whether you have been taking vilazodone or placebo until you leave the study (except in the event of an emergency), decisions about your treatment during the study will not be able to take that information into account.

Other possible risks to you are the side effects that some people get from vilazodone. You should not drive or operate complex or heavy machinery if study medication is affecting your thinking or reflexes. Side effects that may occur include sweating, rash, nausea, vomiting, increased or decreased appetite, weight loss or gain, sleepiness, fatigue, insomnia, dizziness, nervousness, cough, running nose, dry mouth, muscular tremors, changes in heart rate, elevated mood, and sexual problems, including

loss of interest for both sexes, difficulty having orgasm in women, and difficulty having an erection or ejaculating in men. Vilazodone may cause unexpected problems if combined with other medications you might take during the study.

Stopping vilazodone too rapidly may cause dizziness, agitation or anxiety, nausea and sweating. These symptoms usually resolve over time. You should not stop study medication before discussing it with your study doctor.

While vilazodone is considered to be a safe treatment, the Food and Drug Administration (FDA) has issued a public health advisory about a possible link, in rare cases, between suicidal thoughts or behavior in patients treated with antidepressant medications (including vilazodone). The FDA has asked health care providers and patients to note that worsening of depression could be related to the underlying disease process, or in some cases, might be a direct result of antidepressant drug treatment. At the present time, the FDA has not concluded that these drugs cause worsening depressive symptoms or suicidal ideation or behavior, and this is an area of active research. The FDA advisory urges careful monitoring of patients receiving these medications during the beginning stage of therapy and during increases or decreases in dosage.

To minimize risks of study treatment, you have been checked for conditions that can increase risks of treatment, and you will be closely monitored for side effects at every visit. A study doctor will be available by pager 24 hours/day. Your study doctor can adjust the doses of study medications to minimize side effects. If you need to take any other medications during the study, you should first contact your study doctor to minimize the risk of drug interactions. You may leave the study at any time. In the event of a medical emergency, your doctor will be able to find out what medication you have been taking during the study.

For women: **You should not be in this study if you are pregnant.** Women who take vilazodone during pregnancy or who become pregnant while taking it may be at greater risk of having a baby born with a birth defect. You must agree to use birth control

throughout the course of your treatment with medication. If you decide to stop using birth control, or if there is a possibility that you are pregnant during the study, you must tell your study doctor immediately so that a pregnancy test can be done, and we can decide whether you should continue in the study.

Blood Drawing may cause mild discomfort and, rarely, a small arm bruise, clot or infection may occur at the site.
Ratings: You may feel mild to moderate upset or frustration due to answering questions about your life or filling out questionnaires. Study staff are skilled at dealing with these events and will try to help you feel as comfortable as possible (e.g., by giving breaks during an evaluation, offering encouragement).

BENEFITS:

A direct benefit to you is the possibility that the research treatment **may** help your Separation Anxiety Disorder symptoms. In addition, your participation may help researchers learn more about how to treat Separation Anxiety Disorder. There may be no benefit to you if the treatment is not effective.

COMPENSATION:

You will receive $60 for each of the first and last visits, and $30 for each of the **6** interim visits you complete, to be paid in cash after the completion of each visit (up to $300 total), as payment for your time. You will be paid for each of these visits that you complete on schedule, whether or not you are continuing on study treatment.

CONFIDENTIALITY:

All records related to the study are confidential, although state and federal agency, and Forest Laboratories personnel may inspect records. Similarly, there are legal advocacy organizations that have the authority under the law to access otherwise confidential

subject records. They cannot re-disclose this information without the subject's consent. All records will be confidential to the extent permitted by law. Your records will be kept in locked files and access will be allowed only to members of the research team, or institutional personnel as part of a routine audit. Should any of the information gathered from you be used for scientific publications or presentations, you will be protected through the use of a system of codes that will not reveal the identity of individuals. Any report based on this study will only be used as grouped information without mention or description of the individual participants.

Your name and other personal identifying information will be stored in an electronically secure database at New York State Psychiatric Institute. Research data that is entered into the computer will be stored according to study ID number. A master list linking the patient name to the assigned ID number is kept in a separate file. To access the computer and appropriate data files, the staff member must have knowledge of the password and be given rights to access the data by the data manager. All data that is transmitted via computer is encoded and identifying information is removed.

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.

RESEARCH STANDARDS AND PARTICIPANTS' RIGHTS:

Participation in this research study is voluntary. If you decide not to participate, or if you later decide to stop participating, you will not lose any benefits to which you are otherwise entitled. A decision not to participate will not effect your treatment at the New York Psychiatric Institute. The doctors participating in this research study are also responsible for your clinical care in the Anxiety Disorders Clinic, even after you end the study. You will be notified of significant new findings that may relate to your willingness to continue to participate in the study.

Medical Compensation for Research-Related Injuries

Federal regulations require that you be informed about the institution's policy with regard to compensation and payment for treatment of research-related injuries. Short term emergency medical treatment, which has been determined to be necessary by New York State Psychiatric Institute's doctors, and which is within the capability of New York State Psychiatric Institute will be provided. In addition, you will be provided assistance in arranging follow up care in such instances.

New York State Psychiatric Institute and Research Foundation for Mental Hygiene do not provide compensation or payment for treatment of research related injuries. However, you should be aware that participation in this research does not waive any of your legal rights to seek such compensation through the courts.

Dr. Schneier or your study doctor is available to answer your questions about the study at any time. They can be reached during the day at (646) 774-7000. After 5 PM you can page the Anxiety Clinic Doctor on Call at (917) 996-6939. In addition, an emergency psychiatric consultation is always available to you by calling these numbers. The doctors participating in this research study are also responsible for your clinical care. If you have any questions about your rights as a research participant or any complaints, you may call the NYSPI-IRB Main Office at (646) 774-7155 during regular office hours.

You will be given a copy of the signed Consent Form to keep.

STATEMENT OF CONSENT

I voluntarily agree to participate in the research study described above.

NAME_____(print)

Date_____ Signature _____

Study Participant

I have discussed the proposed research with the patient, and in my opinion, this patient understands the benefits, risks and alternatives (including non-participation) and is capable of freely consenting to participate in this research.

NAME_____(print)

Date _____Signature_____

Study Physician

New York State Psychiatric Institute (NYSPI)
Authorization to Use or Disclose Health Information during a Research Study

Protocol Number: 6856 **Principal Investigator:** Franklin Schneier, MD

Name of Study: Vilazodone for Separation Anxiety Disorder in Adults

Before researchers can use or share any identifiable health information ("Health Information") about you as part of the above study (the "Research"), the New York State Psychiatric Institute (NYSPI) is required to obtain your authorization. You agree to allow the following individuals and entities to use and disclose Health Information about you as described below:

- New York State Psychiatric Institute (NYSPI), your doctors and other health care providers, if any, and
- The Principal Investigator and his/her staff (together "Researchers"). Researchers may include staff of NYSPI, the New York State Office of Mental Health (OMH), Research Foundation for Mental Hygiene, Inc. (RFMH), and Columbia University (CU), provided such staff is a part of the study, and
- Providers of services for the Research at CU, NYSPI and/or RFMH, such as MRI or PET, or Central Reference Laboratories (NKI), if indicated in the consent form**.**

1. The Health Information that may be used and/or disclosed for this Research includes:

☑ All information collected during the Research as told to you in the Informed Consent Form.
☑ Health Information in your clinical research record which includes the results of physical exams, medical and psychiatric history, laboratory or diagnostic tests, or Health Information relating to a particular condition that is related to the Research.
☐ Additional information may include:

2. **The Health Information listed above may be disclosed to:**

☑ Researchers and their staff at the following organizations involved with this Research:
New York State Psychiatric Institute

☑ The Sponsor of the Research,
Forest Labs
and its agents and contractors (together, "Sponsor"); and
☑ Representatives of regulatory and government agencies, institutional review boards, representatives of the Researchers and their institutions to the level needed to carry out their responsibilities related to the conduct of the research.
☐ Private laboratories and other persons and organizations that analyze your health information in connection with this study

☐ Other (family members or significant others, study buddies, outside agencies etc.) Specify:

3. By giving permission to release your Health Information as described above, you understand that your Health Information may be disclosed to individuals or entities which are not required to comply with the federal and state privacy laws which govern the use and disclosure of personal Health Information by NYSPI. This means that once your Health

Information has been disclosed to a third party which does not have to follow these laws (e.g., a drug company or the Sponsor of the Research), it may no longer be protected under the HIPAA or NYS Mental Hygiene Law requirements but is subject to the terms of the consent form and may be subject to other state or federal privacy laws or regulations.

4. Please note that:

- You do not have to sign this Authorization form, but if you do not, you may not be able to participate in the study or receive study related care. You may change your mind at any time and for any reason. If you do so, you may no longer be allowed to participate in the study. If you withdraw this Authorization the research staff and the Sponsor, if this is sponsored research, may still use or disclose Health Information containing identifying information they already have collected about you as needed to maintain the reliability of the research. Any request to withdraw this Authorization must be made in writing to (enter name and contact information below):

  Franklin Schneier MD, New York State Psychiatric Institute, Unit 69, 1051 Riverside Drive, New York, NY 10032

- While the Research is going on, you may not be allowed to review the Health Information in your clinical research record that has been created or collected by NYSPI. When this research has been completed you may be allowed to see this information. If it is needed for your care, your Health Information will be given to you or your Doctor.

5. This Authorization does not have an end date.

6. You will be given a copy of this form after you have signed it.

I agree to the use and disclosure of Health Information about me as described above:

_____ _____

Signature of Participant/ Legal Representative Date

_____

Printed Name of Participant

_____

Relationship of Legal Representative to Participant (if applicable)

We also ask you or your legal representative to initial the statements below:

☐ **I have received a copy of the NYSPI/OMH Notice of Privacy Practices.**

Adult Separation Anxiety Study

Are you anxious when separated from your child?
Are you constantly contacting your child?
Worry a lot about harm coming to your child?
Do you worry excessively when your child travels alone?
Do others say you are overprotective?
Avoid activities that involve separation from your child?
Fear being alone?
Are these symptoms interfering with your life?

If you are age 18-60, you may be eligible to participate in a ***research*** study of medication for treatment of Separation Anxiety Disorder in adults. Eligible persons will receive payment for their participation. For more information please contact Rob at (646) 774-8113 or valdovi@nyspi.columbia.edu. All calls are strictly confidential.

***Free Evaluation**

Anxiety Disorders Clinic
New York State Psychiatric Institute/RFMH

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