

# Informed Consent

**Protocol Title:** Acute Antidepressant Therapy in Bipolar II Major Depression

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## **Why am I being asked to volunteer?**

You are being invited to participate in a research study. You are being asked to volunteer since you meet the requirements for enrollment into this study. Your participation is voluntary which means you can choose whether or not you want to participate. If you choose to participate, there will be no loss of benefits to which you are otherwise entitled. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. The research team is going to talk to you about the research study, and they will give you this consent form to read. You may also decide to discuss it with your family, friends, or family doctor. You may find some of the medical language difficult to understand. Please ask the study doctor and/or the research team about this form. If you decide to participate, you will be asked to sign this form.

You have been diagnosed by your doctor as having the symptoms of Bipolar Type II depression. You have been invited to participate in a research study comparing the safety and effectiveness of (1) UPLIFTASE, and (2) LITHIUM CARBONATE (Lithium) in the treatment of Bipolar II depression.

## **What is the purpose of this research study?**

The purpose of this study is to determine if there is a difference in effectiveness between upliftase and lithium in patients with Bipolar Type II depression.

Upliftase is an antidepressant medication which has been on the market in the US since 1997 for the treatment of depression. It has been used by millions of patients world-wide.

Lithium carbonate is a mineral which has been found to be effective in the treatment of Bipolar disorder. It has been on the market in the US since 1970 and has been given to millions of patients world-wide. In many clinical studies, lithium has been shown to be an effective antidepressant and mood stabilizer for patients with Bipolar disorder.

## **How long will I be in the study? How many other people will be in the study?**

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We expect your participation to last for 12 weeks. The entire study is expected to last approximately 18 months in order to enroll all subjects. Eighty-four subjects will be invited to participate from the Depression Research Unit at the University of Pennsylvania.

## **What am I being asked to do?**

### **Prior to study:**

Before starting treatment in this study, you will be required to discontinue your current medication for depression. Depending upon the type of prior medication that you have been taking for your depression, this drug free period could last up to 14 days to assure that you have no drug interaction between the study medication and your prior antidepressant.

### **Tests and Procedures**

Medical history

Physical exam

Urine sample

Electrocardiogram (ECG)

Blood draw to tests to assess Lithium levels - 10 ml (2 teaspoons) each test

### **Initial Visit:**

During the initial evaluation, the following procedures will take place:

- Interviewed by a doctor who will take your medical history and family history. This includes questions about medical illness, medications, allergies, and family history of illnesses
- Written answers to questions about your general health
- General physical examination which is a general examination of your body and generally includes blood pressure reading, heart rate, breathing rate and temperature
- Blood tests for blood chemistry testing: A small needle will be inserted into a vein to collect about 2 teaspoonfuls (10 cc) of blood for testing.
- Urine sample to assess your kidney function and for a drug screen: You will be asked to urinate into a small cup to collect a sample of urine for testing.
- Electrocardiogram (ECG): This is a routine test that involves attaching small wires to your arms, legs and chest to read the electrical impulses of your heart. This test is considered a standard medical test to assess heart function.
- Possible additional clinical tests performed if any of your initial test results are not normal

After the initial evaluation period (lasting up to two weeks), you will be randomly assigned (by a 'toss of the coin') to receive treatment with either upliftase or lithium. Although the assignment of treatment to upliftase or lithium is random (like a toss of the coin), this procedure is used to ensure a fair comparison of the two drugs. Both you and your doctor will know which medication you are receiving.

### **Follow-Up Visits:**

You will be asked to return to the Depression Research Unit (3535 Market Street) for evaluation of your symptoms and treatment after 1, 2, 4, 6, 8, 10 and 12 weeks of treatment. At each of these study visits, the following will occur:

- Examination by your study doctor (or nurse), and your medication dose will be adjusted.
- Series of questions regarding your symptoms and about the presence or absence of side effects
- Blood pressure, pulse and weight measured
- Interviewed about your depression symptoms by a research assistant

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- Return all unused study medication at each visit, and new medication will be dispensed to you.
- Fill out a questionnaire about your general state of health (study visits #2 and #9 only)
- Blood sample 10ml (study visits #3, 4, 5, 7 and 9 only if you are taking lithium)

Your medication dosage will be adjusted gradually upward or downward by your doctor at any time during the study based upon your symptoms, laboratory test results, or the presence of any side effects. The maximum dose of upliftase will be 375 mg daily and the maximum dose of lithium will be 1500 mg daily.

Additional, unscheduled study visits can be arranged if necessary. The average duration of each study visit will be approximately 45 minutes.

## **End of study:**

At the end of 12 weeks of treatment (study termination), one of several things may happen:

- If you and your doctor feel that your depression has improved satisfactorily, you may continue to receive your upliftase or lithium treatment under your primary care doctor's guidance. However, you should be aware that continued treatment with the medication will not be part of the research study, and your treatment and medication will no longer be provided to you without cost.
- If you and your doctor believes that your symptoms have not improved satisfactorily, your doctor will discuss the risks and benefits of other treatments at the Depression Research Unit, or referral for additional treatment.
- If you fail to successfully complete 12 weeks of treatment because you had side effects or you could not tolerate your medication, your doctor will discuss the risks and benefits of other treatments at the Depression Research Unit, or referral for additional treatment.

## **What are the possible risks or discomforts?**

### **Risks from Study Drug**

The most frequent side effects associated with upliftase include nausea, stomach upset, loose stools, headaches, dry mouth, reduced sexual function, insomnia, tiredness, shaky hands, sweating, nervousness, and constipation. On rare occasions, upliftase has been reported to increase blood pressure.

The most frequent side effects of lithium include nausea, loose stools, thirst, increase in urination, hand shakiness, mental dullness, rash, dry skin, decreased thyroid gland function (a gland in your neck involved in body metabolism), and rare cases of kidney damage. Your thyroid gland and kidney function will be checked before your participation in the study, and at the completion of the study.

'Lithium toxicity' occurs when lithium blood levels become too high. Early signs of elevated lithium levels include confusion, unsteadiness when walking, nausea and vomiting. Lithium toxicity is most commonly caused by a reduced salt intake or by excessive sweating. You can easily prevent lithium toxicity by avoiding 'no salt' diets, adding normal amounts of salt to your food, maintaining adequate fluid intake during periods of excessive sweating (e.g., strenuous exercise and flu-like infections). If you should experience any symptoms of lithium toxicity, you should call your doctor immediately.

### **Risks from Study Procedures**

Blood draw: Side effects from having your blood drawn may include discomfort in your arm, fainting, or bruising or infection at the needle puncture site. You must not donate blood while you are participating in the study and up to 10 days after you discontinue taking your medication.

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**Blood Pressure:** The blood pressure cuff does cause the upper arm to be compressed in order for the blood pressure reading to be taken. Some people find the pressure sensation to be uncomfortable. This pressure does not cause any physical damage.

## **Reproductive Risks:**

If you are pregnant or nursing, you should not take part in this research study. We do not know the effects of upliftase or lithium on a fetus, breast-feeding baby, or a mother-to-be and this study could cause serious harm.

- **Female participants:** If you are pregnant, you should tell the study investigator immediately. You will not be included in the study. If you are able to become pregnant, you will be given a urine pregnancy test before starting this study. While taking this study drug, you should not become pregnant. If you do become pregnant, tell your study investigator immediately. During the study and for 6 months following the end of the study you need to take safety measures to prevent pregnancy by not having sex or by using a medically accepted method of birth control such as a diaphragm, cervical cap, condom, surgical sterility, or birth control pills.
- **Male participants:** While you are taking upliftase or lithium you should not father a child. During the study and for 6 months following the end of the study you need to take safety measures to prevent your partner from becoming pregnant by not having sex or by using a medically accepted method of birth control such as a diaphragm, cervical cap, condom, surgical sterility, or birth control pills. If your partner does become pregnant, tell the study investigator immediately.

## **Other Risks:**

You should be aware that there may be additional risks to you while being in this study that are unanticipated. Your condition may not improve, or may worsen while participating in the study. It is also possible that you may experience some discomfort associated with either study drug that has not already been reported.

It is recommended that you avoid drinking any alcoholic beverage while participating in this treatment study.

The study medication must be taken only by the person for whom it has been prescribed. It should be kept out of the reach of children or others of limited capacity to read or understand.

If you experience any troubling side effects or research-related injury, immediately contact your study doctor or study nurse at (215) 665-3665.

## **What if new information becomes available about the study?**

During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

## **What are the possible benefits of the study?**

You will receive the benefit of an evaluation of your depressive symptoms physical examination, laboratory evaluation, ECG, and general health discussions with your study doctor. You may experience the relief or improvement of your depressive symptoms. Your participation may

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benefit other patients with this disorder. However, you may not benefit from participating in this study.

## **What other choices do I have if I do not participate?**

Your participation is voluntary. You can withdraw or refuse to answer any questions without consequences at any time.

There are alternative treatments available to you, including the use of other antidepressant and mood stabilizer medications and psychotherapy. If you agree to participate in this treatment study, you will be given an opportunity to discuss alternative therapies with your study doctor.

If you choose not to participate in this study, or choose to withdraw from the study, your doctor will discuss treatment alternatives for your depression. You do not need to participate in this study to have your depression treated.

## **Will I be paid for being in this study?**

You will not be paid for your participation in this study.

## **Will I have to pay for anything?**

All study-required procedures and the study drugs will be free for you, meaning they will be provided without charge to you. You and/or your health insurance may be billed for the costs of medical care during this study if these expenses would have happened if you were not in the study, or if your insurance agrees in advance to pay.

## **What happens if I am injured or hurt during the study?**

If you have a medical emergency during the study you may contact the Principal Investigator or Emergency contact listed on page one of this form. You may also contact your own doctor, or seek treatment outside of the University of Pennsylvania. Be sure to tell the doctor or his/her staff that you are in a research study being conducted at the University of Pennsylvania. Ask them to call the telephone numbers on the first page of this consent form for further instructions or information about your care.

In the event of any physical injury resulting from research procedures, medical treatment will be provided without cost to you, but financial compensation is not otherwise available from the University of Pennsylvania. If you have an illness or injury during this research trial that is not directly related to your participation in this study, you and/or your insurance will be responsible for the cost of the medical care of that illness or injury.

## **When is the Study over? Can I leave the Study before it ends?**

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped at any time by your physician, the study Sponsor, or the Food and Drug Administration (FDA) without your consent because:

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- The Primary Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The Sponsor, the study Principal Investigator, or the Food and Drug Administration (FDA) has decided to stop the study.

If you decide not to participate, you are free to leave the study at anytime. Withdrawal will not interfere with your future care.

## **Who can see or use my information? How will my personal information be protected?**

The investigator and staff involved with the study will keep your personal health information collected for the study strictly confidential. Please refer to the separate "Confidentiality & Privacy Rights" document that explains more specifically how your personal information will be protected.

## **Who can I call about my rights as a research subject?**

This document explains your rights as a research subject. If you have questions regarding your participation in this research study or if you have any questions about your rights as a research subject don't hesitate to speak with the Principal Investigator listed on page one of this form. Concerning your rights as a research subject, you may also contact the Office of Regulatory Affairs at the University of Pennsylvania by calling (215) 898-2614.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania Health System and the School of Medicine to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania Health System and the School of Medicine to disclose that personal health information to outside organizations or people involved with the operations of this study.

A copy of this consent form will be given to you. You will also be given the University of Pennsylvania Health System and School of Medicine's Notice of Privacy Practices that contains more information about the privacy of your health information.

_____ Name of Subject (Please Print)	_____ Signature of Subject	_____ Date
_____ Name of Person Obtaining Consent (Please Print)	_____ Signature of Subject	_____ Date