

**PRODUCT: LUCEMYRA (Lofexidine)**

**SUBJECT INFORMATION AND CONSENT FORM AND  
AUTHORIZATION TO USE AND DISCLOSE PERSONAL HEALTH  
INFORMATION IN CLINICAL RESEARCH**

**PROTOCOL NUMBER: USWM-LX1-3003-2**

**SPONSOR:**

USWM, LLC (dba US WorldMeds)  
4441 Springdale Rd  
Louisville, KY 40241

**TITLE:**

A Phase 3, Open-Label, Safety Study of Lofexidine

**DOCUMENT DATE:** 16JAN2015

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**Sponsor:** **US WorldMeds, LLC**

**Protocol Number:** **USWM-LX1-3003-2**  
**January 16, 2015 (inclusive of Amendment No. 1)**

**Principal Investigator:**

**Daytime telephone numbers:**

**24-Hour Telephone:**

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**PURPOSE OF THE SUBJECT INFORMATION AND CONSENT FORM**

This Subject Information and Consent Form may contain words you do not understand. Please ask the study doctor or the study staff to explain any words or procedures that you do not clearly understand.

The purpose of this form is to give you information about the research study and, if signed, will give your permission to take part in the study. The form describes the purpose, procedures, benefits, risks, discomforts, and precautions of the research study. You should take part in this study only if you want to do so. You may refuse to take part or withdraw from this study at any time without penalty or loss of benefits to which you are otherwise entitled. Please read this Subject Information and Consent Form and ask as many questions as needed. You should not sign this form if you have any questions that have not been answered to your satisfaction.

**PURPOSE AND DESCRIPTION OF THE RESEARCH STUDY**

You are being asked to take part in a research study of a drug called lofexidine to see if it is useful and safe in reducing opioid withdrawal symptoms in people who are addicted to opioids (for example, heroin and morphine). Lofexidine is a non-addictive drug used in England to decrease symptoms of opioid withdrawal. The Food and Drug Administration (FDA) has not yet approved lofexidine in the United States. Because lofexidine is not FDA approved for treating opioid withdrawal, it is called an investigational drug. In this study we are primarily studying the 3.2 mg dosage strength of lofexidine provided in tablet form for oral administration (by mouth). If you have difficulty tolerating the 3.2 mg dose, you may receive a lower dose of lofexidine (2.4 mg).

You are being considered for participation in this research study because you are addicted to opioids and are seeking treatment for your addiction or you and your doctor wish to change the opioid treatment you are currently receiving. About 250 to 500 subjects at about 20 study sites across the United States will participate in this study. It will take about 4 to 10 months to enroll up to 500 subjects.

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If you participate in this study, you will be required to remain in a clinic setting (hospital, treatment facility, clinic, or clinic-associated housing facility) for the first 3 days of the study where you will take lofexidine 4 times each day (8 AM, 1 PM, 6 PM, and 11 PM). Over the next 4 days (Days 4-7), you will either remain in the clinic setting for treatment with lofexidine or be discharged and treated with lofexidine outside of the clinic (as an outpatient), as determined by you and your study doctor. You may receive lofexidine treatment up to 7 additional days (outpatient only, Days 8-14) if your study doctor decides lofexidine is needed for you to control your withdrawal symptoms. The study will take place over a maximum of 23 days and the total number of days you may receive lofexidine is 14 days.

## STUDY PROCEDURES

### Screening

If you agree to take part in this study, you will first review the consent form and HIPAA (Health Insurance Portability and Accountability Act) document with study staff. You must sign the consent and HIPAA forms before any study-related procedures can be performed, as described below. Screening procedures and/or assessments may require up to 3 clinic visits and the information collected is used to determine if you are eligible to enter the study. If you are not eligible, you will be assisted in finding other substance abuse treatment programs in your geographic area, if you so desire, at your own cost or through your regular health care provider.

- Study staff will ask you a series of questions to check your eligibility to participate against a list of inclusion and exclusion criteria provided by the sponsor.
- Study staff will collect your medical, smoking, and alcohol history and demographic information.
- Study staff will collect your prior medication history (over last 30 days). It is important to tell the study staff all of the medications you are taking, including prescription, nonprescription (over-the-counter medications), opioids of abuse, and herbal preparations.
- A study doctor or designee will complete the Mini International Neuropsychiatric Interview (M.I.N.I.) questionnaire to document your addiction to opioids and any past or current nervous system diseases or mental health illnesses.
- A study doctor or designee will perform a complete physical examination and measure your blood pressure and pulse (while sitting or laying down and standing), respiration rate (breaths per minute) and temperature. Your height and weight will be collected also.
- You will have a blood sample drawn (about  $\frac{1}{2}$  ounce or 3 teaspoonfuls). This blood will show the study doctor how various systems in your body, for example how your liver and kidneys, are working. Some people who have abused opioids for a long time do not have "good veins" even for a single blood draw. If blood cannot be obtained for the required medical tests, you will not be eligible for participation in this study.
- You will have to provide an observed urine sample. Some of this urine will be tested for drugs (like heroin and methadone), some will be used to see how your kidneys and other parts of your body are working, and some used for pregnancy testing as described immediately below.
- If you are female and capable of becoming pregnant, some of the urine collected will be used for pregnancy testing. The result must be negative to participate in the study. If you are able to become pregnant, you must agree to using birth control for the entire duration of this research study. Your study doctor will discuss acceptable forms of birth control.

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- You will be tested for infectious diseases (hepatitis, syphilis, and tuberculosis) and given the results of these tests. If your tuberculosis skin test is positive, you will have a chest x-ray performed to assess active tuberculosis. You will also have a chest x-ray performed if you have previously been positive for tuberculosis. You will not be eligible for study participation if your syphilis or tuberculosis tests are positive, and you will be referred, at your own cost, for appropriate follow-up and/or treatment. You may still be eligible for study participation if you have a positive result for hepatitis but no active liver disease otherwise. The study doctor should know if you have been exposed to a hepatitis virus in the past. A positive result from these tests will be reported to the local health department as required by state law. The results from these tests are confidential and results will not be shared outside of this study except as required by state law. While expected to be confidential, these results, if disclosed, may affect your employment or health insurance options.
- You will have an electrocardiogram (ECG) performed to measure the electrical activity of your heart. This will be done 2 times (8 AM and 11:30 AM) on one day during the screening period.
- You will have a short-term (within the 14-day study period) withdrawal treatment goal defined, for example, abrupt and total withdrawal from heroin, total withdrawal from heroin with assistance with methadone.

### Mandatory In-clinic Treatment (Days 1-3)

For the in-clinic part of this study, you will be required to stay in a unit (hospital, treatment facility, clinic, or clinic-associated housing facility), which may or may not be locked, with or **without visitors**, and you will be required to follow all rules and regulations of the unit. You will be allowed to eat only the food served at the unit (no carry-out). If you are eligible to participate, you will be admitted in time to have the following assessments completed before you receive your first dose of lofexidine at 8 AM on Day 1:

- You will complete the Short Opiate Withdrawal Scale of Gossop (SOWS-Gossop) questionnaire to document the severity of your withdrawal symptoms.
- A study doctor or designee will complete the Clinical Opiate Withdrawal Scale (COWS) questionnaire to document the severity of 11 common opioid withdrawal signs and symptoms.
- A study doctor or designee will complete the Columbia-Suicide Severity Rating Scale(C-SSRS) (baseline version) to document any suicidal thoughts or behaviors over your lifetime.
- A study doctor or designee will perform a physical exam to see if you have any new medical problems since your screening visit.
- A study doctor or designee will measure your blood pressure and pulse (while sitting or laying down; and standing), respiration rate (breaths per minute) and temperature.
- You will have a urine drug screen performed.
- If you are a female capable of becoming pregnant, you will have a urine pregnancy test performed.
- Study staff will ask about any medications you have taken since your screening visit.
- You will have an ECG performed to measure the electrical activity of your heart before the 8 AM dose.

Lofexidine treatment will start after the above procedures confirm you are eligible to participate in this study. You will be given 4 tablets of lofexidine 4 times a day (8 AM, 1 PM, 6 PM, and 11 PM) for 3 days. In all, you will receive 16 tablets each day while in the unit.

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Medicines other than those your doctor gives you are not permitted. Allowed medicines your doctor may give you include nicotine replacement therapy (patch, inhaler, gum, nasal spray) and other medications to treat complaints such as diarrhea; constipation; indigestion and nausea; headache, muscle aches, and other discomforts; cough; and insomnia.

You may be allowed to smoke in the unit, if smoking is permitted in the unit. If you usually smoke tobacco products, the doctors will offer and encourage you to use nicotine replacement medications (for example, nicotine patch, gum, inhaler, or nasal spray) while you are in the unit to treat your nicotine withdrawal symptoms and to make it easier for you not to smoke. If smoking is allowed, smoking breaks outside the in-clinic unit will be constantly observed and supervised.

The following assessments will be completed every day (unless otherwise specified) while you are in the unit on Days 1-3:

- You will complete the SOWS-Gossop questionnaire each day (3.5 hours after the first dose) to document the severity of your withdrawal symptoms.
- A study doctor or designee will complete the COWS questionnaire each day (3.5 hours after the first dose) to document the severity of 11 common opioid withdrawal signs and symptoms.
- A study doctor or designee will complete the C-SSRS (since last visit version) each day (3.5 hours after the first dose) to document any suicidal thoughts or behaviors since the last time the scale was completed.
- A study doctor or designee will assess whether you have completed your pre-defined withdrawal treatment goal.
- Study staff will document any medications you have taken.
- Study staff will monitor you continuously for side effects.
- A study doctor or designee will measure your blood pressure and pulse (while sitting or laying down; and standing, if able) before every dose and 3.5 hours after the 8 AM, 1 PM, and 6 PM doses. Respiration rate and temperature will be measured before the 8 AM dose only.
- A study doctor or designee will perform a complete physical exam 3 to 4 hours after dosing on Day 1 and as clinically needed to monitor your health.
- You will have an ECG performed 3.5 hours after the first dose on Day 1.
- You will have a fingerprick blood sample collected at the same time the ECG is performed on Day 1 (3.5 hours after the first dose).
- You will have blood (about  $\frac{1}{2}$  ounce or 3 teaspoonfuls) and urine samples collected if clinically needed to monitor your health.
- You will have a urine drug screen performed every day.

### In-clinic or Outpatient Treatment (Days 4-7)

As determined by you and your study doctor, you may continue to receive lofexidine treatment in a clinic setting or you can be treated outside of the clinic (outpatient) for the remaining 4 days of mandatory lofexidine treatment (Days 4-7). If you receive lofexidine treatment on an outpatient basis, you will be required to return to the clinic daily before a scheduled dose for the clinical assessments listed below.

The following assessments and procedures will be completed every day (unless otherwise specified) on Days 4-7:

- You will take study medication 4 times a day at 8 AM, 1 PM, 6 PM, and 11 PM.

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- You will complete the SOWS-Gossop questionnaire 3.5 hours after the first daily dose during in-clinic treatment to document the severity of your withdrawal symptoms; if outpatient, this will be completed once daily before dosing.
- A study doctor or designee will complete the COWS questionnaire 3.5 hours after the first daily dose during in-clinic treatment to document the severity of 11 common opioid withdrawal signs and symptoms; if outpatient, this will be completed once daily before dosing.
- A study doctor or designee will complete the C-SSRS (since last visit version) 3.5 hours after the first daily dose during in-clinic treatment to document any suicidal thoughts or behaviors since the last time the scale was completed; if outpatient, this will be completed once daily before dosing.
- A study doctor or designee will assess whether you have completed your pre-defined withdrawal treatment goal.
- Study staff will document any medications you have taken.
- Study staff will monitor you continuously for side effects during in-clinic treatment. If outpatient, you will be asked about any side effects you may have experienced since your last visit.
- A study doctor or designee will measure your blood pressure and pulse (while sitting or laying down; and standing, if able) during in-clinic treatment before every dose and 3.5 hours after the 8 AM, 1 PM, and 6 PM doses. Respiration rate and temperature will be measured before 8 AM dose only.
- A study doctor or designee will measure your blood pressure and pulse (while sitting or laying down; and standing, if able) during outpatient treatment at least once daily before dosing and 3.5 hours after dosing. If you cannot stay in the clinic for the 3.5-hour measurements, you will be given a portable blood pressure machine to measure your blood pressure and pulse at this required time point. You will also be given a paper diary to record these values.
- You will have blood (about ½ ounce or 3 teaspoonfuls) and urine samples collected if clinically needed to monitor your health.
- A study doctor or designee will perform a complete physical exam if clinically needed to monitor your health.
- You will have a urine drug screen performed every day during in-clinic treatment and every day during outpatient treatment.
- You will have a fingerprick blood sample collected each day during outpatient treatment.
- If outpatient, you will be given a paper diary to record the time of dosing for each of the 4 required daily doses; to record blood pressure and pulse if not recorded during the in-clinic visit; and to record any symptoms of hypotension (low blood pressure) or bradycardia (low pulse), as listed in the paper diary.
- If outpatient, you will need to return the dispensed study medication bottles and study diary every day when you return to the clinic so the study staff can account for all study medication.

After 7 days of lofexidine treatment, your study doctor will decide if you still need lofexidine to control your withdrawal symptoms. If not, you will be discharged from the study after at least one dose on Day 7 and all end-of-study procedures have been completed. If your study doctor decides you need to continue lofexidine treatment, you may receive lofexidine treatment on an outpatient basis only (see below).

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### **Outpatient Only Treatment (Days 8-14)**

As determined by your study doctor, you may continue lofexidine treatment on an outpatient basis only for up to an additional 7 days to control your withdrawal symptoms. Lofexidine dosing may be stopped at any time during Days 8-14. You will be required to return to the clinic daily before a scheduled dose for the clinical assessments listed below.

The following assessments and procedures will be completed every day (unless otherwise specified) on Days 8-14:

- You will complete the SOWS-Gossop before dosing.
- A study doctor or designee will complete the COWS questionnaire before dosing.
- A study doctor or designee will complete the C-SSRS (since last visit version) before dosing.
- A study doctor or designee will assess whether you have completed your pre-defined withdrawal treatment goal.
- Study staff will document any medications you have taken.
- Study staff will ask you about any side effects you may have experienced since your last visit.
- A study doctor or designee will measure your blood pressure and pulse (while sitting or laying down; and standing, if able) at least once daily before dosing and 3.5 hours after dosing on Days 8-13 and once before any dose on Day 14. If you cannot stay in the clinic for the 3.5-hour measurements, you will be given a portable blood pressure machine to measure your blood pressure and pulse at this required time point. You will also be given a paper diary to record these values.
- You will have blood (about  $\frac{1}{2}$  ounce or 3 teaspoonfuls) and urine samples collected if clinically needed to monitor your health.
- A study doctor or designee will perform a complete physical exam if clinically needed to monitor your health.
- You will have a urine drug screen performed every day.
- You will have a fingerprick blood sample collected every day.
- You will be given a paper diary to record the time of dosing for each of the 4 required daily doses; to record blood pressure and pulse if not recorded during the in-clinic visit; and to record any symptoms of hypotension (low blood pressure) or bradycardia (low pulse), as listed in the paper diary.
- You will need to return the dispensed study medication bottles and study diary every day when you return to the clinic so the study staff can account for all study medication.

### **Study Discontinuation/End of Study**

When you complete or if you are removed from the study for any reason, you will have the following assessments completed after your last dose of study medication:

- A study doctor or designee will complete the COWS and C-SSRS questionnaires.
- A study doctor or designee will assess whether you have completed your pre-defined withdrawal treatment goal.
- You will complete the SOWS-Gossop.
- Study staff will ask about any medications you have taken and any side effects you may have experienced since your last visit.

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- You will have an ECG performed before your last dose and after dosing.
- A study doctor or designee will perform a complete physical examination and measure your blood pressure and pulse (while sitting or laying down; and standing, if able), respiration rate, temperature, and weight.
- You will have blood (about ½ ounce or 3 teaspoonfuls) and urine samples collected to document your overall health.
- If you are a female of childbearing potential (capable of being pregnant), you will have a urine pregnancy test.
- You will have a urine drug screen performed.
- If you are being treated as an outpatient, you will need to return the dispensed study medication bottle when you return to the clinic so the study staff can account for all study medication.

Study staff will contact you by telephone 30 days after your last dose of study medication to ask you about your current treatment status (for example, current psychosocial treatment, relapse, or successful entry into another substance abuse treatment program) and any side effects you may have experienced since your last visit.

### **SUBJECT OBLIGATIONS**

If you are a female and capable of becoming pregnant, you must use birth control during your participation in the study. You can discuss birth control options with your study doctor.

You will be allowed to take medications during the study, as necessary, for example, nicotine replacement therapy (patch, inhaler, gum, nasal spray) and medications to treat complaints such as diarrhea (e.g., Pepto-Bismol, Imodium); constipation (e.g., dioctyl sodium sulfosuccinate and psyllium hydrocolloid suspension); indigestion and nausea (e.g., Alumina, Magnesia, and Simethicone); headache, muscle aches, and other discomforts (e.g., Tylenol, Advil); cough (e.g., guaifenesin); and insomnia (e.g., zolpidem, trazadone). It is very important that you discuss with the study doctor before you begin taking any other prescription or nonprescription (over-the-counter) medications, or herbal preparations to make sure they are acceptable to take with the study drug. Some drugs may have dangerous interactions with lofexidine, as described further in the section immediately below.

### **RISKS OR DISCOMFORTS**

Lofexidine, as an investigational drug, may involve some risks to you that are currently unknown. Your opioid withdrawal symptoms may improve, not change, or may worsen if you take part in this research study.

There is a chance that you may experience opioid withdrawal symptoms during the study including nausea, vomiting, diarrhea, muscle pain, abdominal discomfort, sweating, runny nose, watery eyes, restlessness, tremors, chills, increased heart rate and blood pressure, and agitation.

You may experience some side effects from the study drug. Lofexidine, at the doses planned in this study, may cause a decrease in blood pressure and pulse and cause dizziness, especially when you stand up too quickly. After the study drug is discontinued, you may experience a temporary increase in blood pressure.

You may also experience drowsiness and/or dry mouth, nose, or throat while taking lofexidine. Other rare side effects of lofexidine that have been reported by less than 5% of subjects in other completed trials, which are listed in the Investigator's Brochure for lofexidine, may include trouble breathing, very

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slow heart rate, severe skin rash, faintness, unusual tiredness or extreme weakness, constipation, or loss of appetite. There are also some reports of the QTc interval of the heart being too long in people taking lofexidine. The QTc interval is a measurement on an ECG reading that shows the electrical activity in the heart's lower chambers, the ventricles. When the careful timing of the heart's patterns are upset or disrupted and the QTc interval is longer than usual; it can lead to fainting, heart attack, or sudden death. There was one report of a person who experienced Torsades de Points, a potentially fatal abnormal heart rhythm (although this patient recovered and it was not clear if lofexidine was responsible for the event). Torsades de Pointes is an irregular heartbeat caused by the heart's lower chambers beating faster than usual, causing less blood to pump out of the heart, which leads to sudden fainting. If the episode is short, the heart can correct itself on its own. If an episode of Torsades de Points persists, however, it can lead to an irregular heartbeat known as ventricular fibrillation (a condition causing the lower chambers of the heart to beat so fast that the heart shakes and stops pumping blood) and possibly death.

You should be aware that you will probably be more sensitive to the effects of heroin and other opioids after you complete this study. You should be extremely careful after you leave the study, if you decide to use opioids again. Any opioid, even at doses you took in the past, could cause an overdose, severe medical problems, or even death.

Risks associated with drawing blood from your arm or by finger stick include pain, bruising, lightheadedness and, on rare occasions, infection. Precautions will be taken to minimize these risks. The total amount of blood that you will be asked to give during the study is about 1.2 ounces (7.2 teaspoons). This is much less than a unit of blood (about 16 ounces) typically given during a blood donation.

Some drugs may have dangerous interactions with lofexidine and should not be used together. Using lofexidine and beta-receptor blockers (to treat high blood pressure) together may cause a very low heart rate. Using lofexidine with alcohol, sedatives, and/or antihistamines may enhance central nervous system depressant effects (for example excessive sleepiness). Before starting any new medications, you should talk with your study doctor.

Nicotine Replacement Medications: You should not smoke if you are being treated with nicotine replacement medications since this may result in high levels of nicotine in your blood. Signs and symptoms of high levels of nicotine in your blood are nausea, vomiting, abdominal pain, diarrhea, weakness, dizziness, loss of color, cold sweats, tremor, mental confusion, headache, and disturbed hearing and vision.

In addition to the risks or discomforts listed above, there may be other risks that are currently not known. Also the risks or discomforts described may occur more often or be more severe than has been seen before.

## REPRODUCTIVE RISKS

The effects of lofexidine on the human fetus are unknown. High doses of lofexidine given to pregnant mice, rats, and rabbits caused a reduction in fetal weights and slight increase in fetal resorptions (loss of fetus with the fetus absorbed within the pregnant animal's body). If you become pregnant while in this research study, an injury to the fetus may occur that has not been seen before. Additionally, the effects on an infant, through breast feeding (nursing), are unknown.

If you become pregnant during the study or within 30 days after study completion, notify your study doctor immediately. Your pregnancy will be followed to outcome.

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### **NEW FINDINGS**

Your study doctor will tell you of any information learned during the course of the study that might cause you to change your mind about taking part in this research study. You may contact the study doctor at any time after your participation ends to find out if any new information about this study has become available.

### **POSSIBLE BENEFITS**

Your opioid withdrawal symptoms may be reduced while participating in this study but we cannot guarantee that you will receive any benefits by taking part in this study. Your participation in the study will contribute to information about this non-addictive study drug and may benefit other patients addicted to opioids in the future.

### **PAYMENT TO SUBJECT FOR PARTICIPATION**

For your participation, you will be paid for your time and inconvenience as follows:

Screening (up to 3 visits):

Days 1-3 (In-clinic):

Days 1-7 (In-clinic):

Days 4-7 (Outpatient)

Days 8-14 (Outpatient):

The maximum compensation you may receive for your participation in this research study is \_\_\_\_\_, in the event you require 3 screening visits, you receive in-clinic treatment on Days 1 through 7, and you participate through Day 14.

If you require transportation for clinic visits, you may be reimbursed for expenses (after you submit receipts) or transportation may be provided by the study site.

You will receive compensation by cash, check, or vouchers in accordance with your local study site's policies.

### **COSTS**

You do not have to pay for your stay in the unit, study visits, and for any treatment or testing done as part of this research study.

### **ALTERNATIVE TREATMENTS**

No non-opioid drugs are currently approved by the U.S. FDA for the treatment of opioid withdrawal signs and symptoms. You do not have to take part in this research study, however, to receive treatment for your condition. If you decide not to take part in this study, a study doctor will discuss alternative treatments with you. Two prescription drugs (buprenorphine and methadone) are available to treat your withdrawal symptoms. Both of these drugs are opioids and have side effects and risks associated with their use. Individual and/or group counseling may also help your condition. The study researchers will, at your request, refer you to public or private substance abuse treatment programs in your geographic area, at your own cost or through your regular health care provider. Refusal to participate in this study will not affect other medical care for which you may be eligible.

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### **CONFIDENTIALITY AND RELEASE OF MEDICAL RECORDS**

We will protect information about you and your taking part in this research study to the best of our ability. To help protect your privacy, the study sponsor (US WorldMeds) has obtained a Certificate of Confidentiality from the National Institutes of Health (NIH). With this certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings.

The Certificate of Confidentiality does not prevent the researchers, however, from disclosing voluntarily, without your consent, information that would identify you as a participant in the research study under certain circumstances (for example, abuse, neglect, harm to self, harm to others, and certain cases of communicable diseases). In addition, absolute confidentiality cannot be guaranteed because medical records and study information that identify you may need to be audited or evaluated by authorized staff from the U.S. FDA, Institutional Review Board (IRB), the study sponsor (US WorldMeds), and other health authorities to meet their specific requirements.

These agencies and researchers are bound by rules of confidentiality, however, and they make every effort not to release information that identifies you. If information about this study is published, your name, initials, or any other identifying information will not be given.

Data collected during the study (including laboratory specimens, medical records, and other data forms and records) will be stored in a way that does not identify you by name. Research and clinical records will be stored in a locked cabinet. Only selected study researchers will have access to this information and they are bound by rules of confidentiality not to reveal identifying information to others.

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 RELATED INJURY**

If you are injured as a result of the study drug or study procedures performed during your inpatient participation in this research study, you will receive medical care at the study site or an emergency department as clinically necessary.

If you are injured as a result of the study drug or study procedures performed during your outpatient participation in this research study, you should seek medical attention at the health care provider of your choice or an emergency department if necessary. The sponsor or study site will cover the medical expenses necessary to treat the injury only to the extent that such costs are not covered by your health insurance policy, by a government program, or by any other third party.

You must follow the directions of the study doctor to be eligible for this coverage.

Neither the sponsor nor the study doctor/study site has a program in place to provide other compensation in the event of an injury.

### **LEGAL RIGHTS**

You do not waive any legal rights by signing this Subject Information and Consent Form.

### **VOLUNTARY PARTICIPATION**

Your decision to take part in this research study is completely voluntary. There will not be any penalty or loss of benefits to you if you decide not to take part. You will be informed of any significant new

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information that becomes available during the course of the study that might affect your decision to continue your participation in the study.

You may drop out of this study at any time. Because there may be risks associated with this decision, you should inform the study staff. They will assist you in properly ending your participation, including returning to the clinic for tests if you are an outpatient.

If you leave the study early, you will be assisted in finding other substance abuse treatment programs in your geographic area, if you so desire, at your own cost or through your regular health care provider.

## WITHDRAWAL

Your doctor, the sponsor company, or the FDA has the right to stop your participation in the study at any time, with or without your consent, for any of the following reasons: if you have an adverse effect from the study drug; if you need a treatment not allowed in this study; if you fail to follow the study procedures; if you become pregnant; or if the study is canceled by the FDA or the sponsor company. The sponsor may decide to stop the study and your access to the study under certain circumstances, even if the study drug appears to be safe and effective. You may drop out of this research study at any time, without penalty (see above).

## **CONTACT FOR QUESTIONS**

If you have any questions about your participation in this research study, or if you feel that you have experienced a research-related injury or reaction to the study drug, contact the study doctor at the telephone number listed on page 1 of this form.

This study was reviewed by An IRB reviews research to protect the rights and welfare of study participants. If you have problems, concerns, suggestions, questions or information about the study, and for information regarding research subject's rights, please call (toll free).

Although [REDACTED] has approved the information provided in this informed consent form and has granted approval for the investigator to conduct the study this does not mean [REDACTED] has approved your participation in the study. You must evaluate the information in this informed consent form for yourself and decide whether or not you wish to participate.

## **AUTHORIZATION TO USE AND DISCLOSE PERSONAL HEALTH INFORMATION FOR RESEARCH**

The United States government has issued a new privacy rule to protect the privacy rights of patients. This rule was issued under a law called the Health Insurance Portability and Accountability Act of 1996 (HIPAA). The Privacy Rule is designed to protect the confidentiality of your personal health information. The document you are reading, called an "Authorization," describes your rights and explains how your health information will be used and disclosed (shared).

In working with the sponsor, the study doctors will use and share personal health information about you. This is information about your health that also includes your name, address, telephone number, or other facts that could identify the health information as yours. This includes information in your medical record and information created or collected during the study. This information may include results of your medical history, physical exam, and laboratory tests (blood, urine, and ECG). Some of these tests may have been done as part of your regular care. The study doctor will use this information about you to complete this research.

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In most cases, the study doctor will use your initials and assign a code number to your information that is shared with the sponsor. The sponsor and its representatives may review or copy your personal health information at the study site. Regulatory authorities and the IRB may also review or copy your information to make sure that the study is done properly or for other purposes required by law.

By signing this Authorization, you allow the study doctor to use your personal health information to carry out and evaluate this study. You also allow the study doctor to share your personal health information with:

- the sponsor and its representatives;
- 
- the U.S. FDA; and
- other regulatory agencies.

Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the Privacy Rule. These groups, however, are committed to keeping your personal health confidential.

You have the right to see and get a copy of your records related to the study for as long as the study doctor has this information. By signing this Authorization, however, you agree that you might not be able to review or receive some of your records related to the study until after the study has been completed.

You may choose to withdraw this Authorization at any time, but you must notify the study doctor in writing. Give your written withdrawal notice to your study doctor if you are being treated as an inpatient. If you are being treated as an outpatient, send your written withdrawal notice to the study doctor at the address listed on page 1 of this form.

If you withdraw from the study and withdraw your Authorization, no new information will be collected for study purposes unless the information concerns an adverse event (a bad effect) related to the study. If an adverse event occurs, your entire medical record may be reviewed. All information that has already been collected for study purposes, and any new information about an adverse event related to the study, will be sent to the study sponsor.

If you withdraw from the study but do not withdraw your Authorization, new personal health information may be collected until this study ends.

This authorization does not have an expiration date. If you do not withdraw this Authorization in writing, it will remain in effect indefinitely. Your study doctor will keep this Authorization for at least 6 years.

If you do not sign this Authorization, you cannot participate in this research study or receive study-related treatment. If you withdraw this Authorization in the future, you will no longer be able to participate in this study. Your decision to withdraw your Authorization or not to participate will not involve any penalty or loss of access to treatment or other benefits to which you are entitled.

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**VOLUNTEER'S STATEMENT:**

**A Phase 3, Open-Label, Safety Study of Lofexidine**

I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. I may contact the study doctor if I have any more questions about taking part in this study. The study doctor or the company he/she is employed by is being paid by the sponsor for my participation in this study.

I understand that my participation in this research project is voluntary. I know that I may quit the study at any time without harming my future medical care or losing any benefits to which I might be entitled. I also understand that the investigator in charge of this study may decide at any time that I should no longer participate in this study.

If I have any questions about my rights as a research subject in this study I may contact \_\_\_\_\_ at \_\_\_\_\_ (toll free).

By signing this form, I have not waived any of my legal rights.

I have read and understand the above information. I agree to participate in this study. I understand that I will be given a copy of this signed and dated form for my own records.

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Study Participant (signature)

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Date

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Print Participant's Name

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Person who explained this study (signature)

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Date