

Partners HealthCare System Research Consent Form

Subject Identification

General Template

Version Date: November 2005

Protocol Title: BLOOM-DM: Behavioral modifications and Lorcaserin for Overweight and Obesity Management in Diabetes Mellitus -- A 52-Week, Double-blind, Placebo-controlled, Parallel-group Study to Assess the Safety and Efficacy of Lorcaserin Hydrochloride in Overweight and Obese Patients with Type 2 Diabetes Mellitus Managed with Oral Hypoglycemic Agent(s)

Principal Investigator: Lee M. Kaplan, MD, PhD

Site Principal Investigator:

Description of Subject Population: Overweight or obese adults with type-2 diabetes mellitus

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called “subjects.” This term will be used throughout this consent form. If you have any questions about the research or about this form, please ask us. If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a copy of this form to keep.

Why is this research study being done?

We are studying an “investigational” drug, lorcaserin hydrochloride (“lorcaserin”), formerly known as APD356. An investigational drug is one that has not been approved by the United States (US) Food and Drug Administration (FDA) for sale. Arena Pharmaceuticals, the company that makes lorcaserin is sponsoring (paying for) this study.

Your main study visits will be conducted at the **MGH Weight Center**. The clinic is located at **50 Staniford St, 4th Floor, Boston, MA 02114**.

This is the tenth study using lorcaserin in humans. It’s the seventh study in which lorcaserin pills are given to obese patients for more than one day. More than 4300 volunteers have taken part in studies of lorcaserin so far. The studies have ranged from single doses up to 52 weeks of dosing.

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The main purpose of this study is to find out the effects of lorcaserin in obese and overweight subjects. Our subjects have one or more complications caused by their weight. Another purpose of this study is to gather information about how safe lorcaserin is.

We will also use a placebo in this study. A placebo looks exactly like the active study drug but contains no active ingredients. Placebos help us know if the study results are from the study drug or from other reasons. Subjects in this study will take study drug or placebo and will also follow a diet and exercise program for one year.

We expect to enroll about 25 subjects at MGH, out of a total study enrollment of about 750 subjects. This study will take place at about 40 different medical centers across the US.

Background Information: Other obesity drugs

Lorcaserin is being developed as a possible treatment for obesity. More than 1 billion individuals worldwide are overweight. At least 300 million of these people are obese. This is more than 20% of the world population. In the U.S., about 30% of adults and 15% of children and adolescents are considered obese and many more are overweight.

Obesity can lead to other diseases and conditions. These include high blood pressure, high cholesterol, diabetes, sleep disorders, arthritis, and some cancers. The treatment of obesity includes diet and exercise programs, treatment with drugs, and surgery (for some extreme cases).

Only two prescription drugs are currently approved in the U.S. for the chronic treatment (longer than 12 weeks) of obesity. These drugs are sibutramine (Meridia[®]) and orlistat (Xenical). Also, phentermine is approved in the U.S. for short-term use (less than 12 weeks). Phentermine is sold in the U.S. under the brand names Adipex[®] and Ionamin[®]. However, use of these drugs is limited. They work only moderately well and have unwanted side effects. Side effects include increased blood pressure (Meridia), stomach and intestinal side effects (Xenical), and possible addiction (phentermine).

Lorcaserin is meant to be used along with diet and exercise to achieve weight loss. Lorcaserin works in a way that is similar to two older appetite-suppressing drugs. Those drugs are called fenfluramine and dexfenfluramine. In 1997, fenfluramine (Pondimin[®]) and dexfenfluramine (Redux[®]) were withdrawn from the market in the US due to safety concerns. These concerns included damage to heart valves and pulmonary hypertension. Lorcaserin was designed to try to overcome these dangerous side effects but to retain the weight loss effects.

At this time, we don't fully understand the cause of the side effects that made Pondimin[®] and Redux[®] unsafe. We also don't fully understand the side effects of lorcaserin itself. For this reason, we cannot be sure that the harmful effects have been eliminated. You may experience side effects, which you should report to your study doctor.

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How long will I take part in this research study?

This research study begins with a 6-week screening period to see if you qualify for the study. After screening, there is a 52 week dosing period, when you will take the study drug. You will make at least 2 outpatient visits during the screening period and at least 15 outpatient visits during the dosing period. Your study doctor may ask you to make extra visits for safety reasons.

We will also make a follow-up telephone call to you about 4 weeks after your last visit to check on your health.

What will happen in this research study?

At your first screening visit, you will read this consent form and have the opportunity to ask questions about the study. If you agree to take part, you will sign and date the consent form. Then we will do some tests and procedures to see if you qualify for the study.

First Screening Visit:

(This visit will take about 2 hours)

At this visit we will do the following procedures:

- Medical history, including tobacco, alcohol and caffeine use
- Physical examination, including measuring your height, weight, and vital signs (blood pressure, heart rate and oral temperature).
- Electrocardiogram (ECG). A test to measure the electrical activity of your heart. We will put small, sticky pads (called electrodes) on your chest, arms, and legs. The pads are attached to wires, which are connected to a machine that will measure your heart rhythm. Blood sample for routine laboratory testing, screens for hepatitis B and C, screen for HIV. About 4 teaspoons of blood will be collected. If you test positive for HIV, hepatitis B, or hepatitis C, we may have to report this information to the responsible governmental agency. The results of these tests will not become part of your medical record. If these tests are positive, you cannot be in the study.
- Urine sample for routine laboratory testing and screening for drugs of abuse such as heroin, cocaine or oxycontin (must be negative to enter study). Results of these tests will not be entered into your medical records.
- Blood pregnancy test for female subjects (must be negative to enter study)
- Several screening questionnaires
- Review of the entry requirements for the study.

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We will ask you to fill out screening questionnaires about your general mental health and eating habits. These questionnaires should take about 10 to 15 minutes to complete. While we hope that you will answer all of the questions, you can skip any questions you don't want to answer. However, if you skip any question on these questionnaires, they will be considered incomplete and you will not be permitted to enter this study. Your responses to these questionnaires will not become a part of your medical record.

Baseline echocardiogram

(This visit will take about 1 hour)

If the first set of tests and procedures show us that you qualify for the study, you will have a second screening visit. We will give you an echocardiogram, which will take about 1 hour. An echocardiogram is a test that uses sound waves to create a moving picture of the heart. The picture is much more detailed than an x-ray image. It does not involve any radiation exposure, like an x-ray does.

A technician performs the test, and then a cardiologist (heart doctor) evaluates the results. The technician will place an instrument called a transducer probe on your chest, near the breast bone. The probe sends out sound waves, which are directed toward the heart. The sound waves make a picture on a nearby screen of the activity of your beating heart.

You will take all your clothes off above the waist and will lie on an examination table on your back. The technician will place electrodes onto your chest and will spread a gel on the skin of your chest. Then the technician will move the transducer over the skin with gel on it. You will feel slight pressure on your chest from the transducer. The technician may ask you to breathe in a certain way or to roll over onto your left side to get a better view of your heart.

The results of the study echocardiograms will not become a part of your medical record.

Electrodes will be placed onto your chest to allow an ECG to be performed during the echocardiogram procedure.

For the purposes of this study, the echocardiograms will be read at Biomedical Systems by trained, licensed cardiologists. You may be referred to a cardiologist if a problem is found on the echocardiogram.

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Day 1 (the first day you take the study drug or placebo)

(This visit will take about 3 hours)

After all test results are in, we will do a final check to see if you still qualify for the study. If so, we will ask you to come in to the MGH Weight Center. This will be Day 1 of the dosing period of the study.

We ask that you fast for 10 full hours before your appointment. Fasting means not eating any food or drinking any beverage except water during those 10 hours. We will collect blood and urine samples for routine laboratory tests.

Before we give you any study drug on Day 1, we will do the following things:

- Evaluation of any changes to your health since the last visit
- Check of other drugs you are taking
- Measure your weight and waist and hip circumference (distance around)
- Measurement of your vital signs (e.g., blood pressure, heart rate, and body temperature)
- Urine pregnancy test
- Quality of Life Questionnaire

If you are a female, we will ask you about your reproductive status (i.e. pre-menopausal, post-menopausal). If you are able to become pregnant, we will record your current method of birth control and the start date of your last menstrual cycle.

Diet and exercise counseling

You will meet with the dietitian for the first time on Day 1. The dietitian will introduce the Arena Healthy Lifestyle program to you. Throughout the study you will be asked to complete a log of what you eat and how much you exercise. You should try to complete this log as much as possible and bring it with you at every visit. The log should take less than 5 minutes to complete. See page 8 of this consent form for additional information about the nutrition program.

Monitoring your blood sugar level

You will be provided with a (OneTouch® Ultra® 2, LifeScan, Inc., Johnson & Johnson) glucose (blood sugar) monitor at Day 1. The research nurse will train you to perform fingerstick glucose measurements. You will be required to perform glucose self-monitoring at least twice daily. You will be asked to perform a fingerstick before breakfast (fasting) and before dinner; pre-lunch and bedtime monitoring are also

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encouraged but not required. You should also measure your glucose if you feel like you have very low blood sugar (hypoglycemic). If you have low blood sugar you will feel light-headed, nauseous and/or disoriented.

Taking the Study Drug or Placebo

During the study drug period, you will be assigned to one of three groups:

- placebo or
- lorcaserin (10 mg) tablets once-a-day (QD), or
- lorcaserin (10 mg) tablets twice-a-day (BID).

You will take the study drug for 52 Weeks. Two out of 3 subjects will take lorcaserin, and 1 out of 3 will take placebo. You and the study doctors cannot choose your group.

This study is called a “double-blinded” study. This means neither you nor your study doctor will know whether you are receiving placebo or lorcaserin. However, in case of an emergency, this information is available to the study doctor.

After we complete all the Day 1 procedures, you will receive a single dose of your assigned study drug (lorcaserin or placebo) with a full glass of water. We ask that you stay at the MGH Weight Center for about 2 hours after dosing, so we can watch you carefully for any side effects. We do not know all the side effects that could possibly occur with the study drug. When you leave, you should be careful in going about your daily routine, including driving or operating heavy machinery, until you know how the drug affects you.

After about 2 hours, we will measure your vital signs and we will draw a small sample of blood to measure hormone levels in your blood.

After all procedures are completed, and we have watched you for 2 hours, you can leave the clinic. We will give you a supply of lorcaserin or placebo to last until your next visit.

You will take a capsule without food about 1 hour before your morning meal and about 1 hour before your evening meal. Your next appointment will be for about 2 weeks later (Week 2).

We will remind you not to take any other medications without the study doctor’s approval. This includes both prescription drugs and drugs bought over the counter.

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Please call us right away if you experience any side effects or other changes in your health or well-being. We will give you these reminders and instructions at every visit.

Study Visit Weeks 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, and 52

The visits will take between 1½ to 2½ hours.

We ask that you return to the hospital for study visits during Weeks 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, and 52 for tests to see how you are doing.

During all study visits, the following tests will be done:

- Urine pregnancy tests for women
- Measurement of vital signs
- Measurement of weight
- Diet and exercise counseling
- Check of study drug to ensure you are taking it correctly
- Check of other drugs you are taking
- Evaluation of any side effects you might have had.

Certain additional procedures will be done at certain visits. Here is a listing of those study procedures:

- On Weeks 2, 4, and 36 you will report to the MGH Weight Center at the appointed time. Because blood and urine samples will be collected for routine laboratory tests, you will be asked to fast (no food or liquid, except water) overnight (or for 10 hours) before coming for these visits.
- At Week 4, you will also be given questionnaires about how you feel and have a complete physical exam.
- Your next appointment will be scheduled, and you will be reminded not to take any other medications without prior approval from the study doctor. We will also remind you to call if you experience any significant changes in your well-being.

Weeks 12, 24 and 52

The visits at Weeks 12, 24, and 52 will require that you return to the clinic 3½ to 6 hours after the visit for a blood draw. The follow-up blood draw will take 10 minutes. In addition to fasting prior to these visits, you should not take your regular morning dose of study medication on the morning of the Weeks 12, 24 and 52 visits. Your morning dose should be taken at the study site as instructed by study staff.

- You will take your morning dose after we have collected lab samples to measure the

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amount of study drug and hormone levels in your blood (pharmacokinetics). Labs will be collected again approximately 1 ½ hours after the dose. We will then ask you to return to the clinic between 3 ½ and 6 hours after the first dose for a final blood draw.

- After all procedures for these visits have been completed, you will be given study drug (lorcaserin or placebo) so you can continue to take it as directed.
- At Weeks 24 and 52, you will also be given questionnaires about how you feel and have an echocardiogram and a complete physical exam. During these visits, we will also measure waist and hip circumference (distance around).

Week 56 (Telephone call)

A member of the study staff will call you to discuss how you are doing since the study ended. The telephone call will take about **20** minutes. If you have had any problems since stopping the study drug or placebo, please tell the study staff member during this call. After this phone call, your time in the study will be over.

General Study Information

Taking Other Medications During the Study

- You may not be able to be in the study if you have taken certain medications.
- You must agree not to take any drug unless approved by the study doctor while you are in this study. This includes both prescription drugs and drugs and herbal supplements bought over the counter. With all medications, failure to follow dosage instructions may result in adverse (harmful or unwanted) side effects.
- You should talk to your primary care doctor and the study doctor before stopping or reducing doses of any prescribed medicines you are currently taking.

Your Diet During the Study

- You should not eat poppy seeds or foods containing poppy seeds for at least 24 hours before attending any visit requiring urine sampling for drugs of abuse. These foods may give a false test result, the same as if you have used opiate drugs, such as oxycontin or heroin.

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- You will be required to fast overnight (10 hours) before each study visit requiring a blood sample for laboratory tests.
- You will be required to follow the diet program (Arena[®] Healthy Lifestyle Program) as prescribed by your study dietitian/counselor. We will work with you while you are in the study to help you follow the program and to support you in making lifestyle changes. These lifestyle changes can help you lose weight and keep the weight off. The program will focus on fitting healthy eating and moderate physical activity into your daily life.
- You cannot be in this study if you have a history of binge eating.

Physical Activity and Exercise During the Study

- You will participate in the Arena[®] Healthy Lifestyle Program diet and exercise program designed just for this study. You must follow the program in order to be in this study. The program will require that you meet with a dietitian/counselor, who will guide you through healthy eating and activity schedules.
- At your first interview with the counselor/dietitian, which will last about 1 hour, he or she will ask you for information about your eating and exercise habits. The counselor/dietitian will use this information to create a program especially for you. The diet requires you to eat about 600 kilocalories (“calories”) less than what would be required to maintain your current body weight. (A large order of French Fries has about 600 calories.) After the initial visit, you will meet with the counselor/dietitian at regular visits to discuss your progress on the program and make any adjustments.

Smoking During the Study

You may not be able to be in the study if you use tobacco. The study doctor will decide if you can take part in this study.

Leaving the Study Early

You are volunteering to be in this research study. You are free to leave the study at any time. You may choose to leave the study or not take part in the study without penalty or losing any benefits due to you. If you leave the study, you will be told of the required steps you should follow for your health and safety. You may be asked to complete final laboratory tests and examinations to be scheduled at a later date. The last visit will follow the same procedures described in Week 52 above. You must also return all study drugs.

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The study doctor, the sponsor, or the FDA can remove you from the study without your consent. Reasons for removal may include but are not limited to:

- If you have any change in your medical condition which might be harmful to you;
- If you have severe or unacceptable side effects;
- If you fail to follow the study instructions;
- If the study doctor feels that it is best for you not to participate or continue in the study;
- If the study is stopped for any reason.
- If you become pregnant.

If you withdraw from the study early, the following exit procedures will be performed:

- weight measurement,
- waist circumference,
- physical exam,
- answer questions about how you feel,
- collection of blood and urine samples for clinical laboratory tests,
- ECG,
- quality of life assessment, and
- assessment of any side effects.

You may also have an echocardiogram. A member of the study staff will call you 4 weeks after your last dose of study drug to discuss any side effects. We will try to obtain your body weight measurement at the scheduled time of your Week 52 visit, even if you have missed other visits.

Echocardiograms if you leave the study early

If you discontinue, we will ask you to have an echocardiogram as follows:

- Prior to Week 24 Visit: We will do an echocardiogram when you exit the study. We will ask you to have an additional echocardiogram at the time of the Week 52 visit.
- After the Week 24 echocardiogram, but prior to the Week 36 visit: The Week 24 echocardiogram will serve as the exit echocardiogram. We will ask you to have an additional echocardiogram at least 3 months after the Week 24 echocardiogram. (This would be no sooner than the intended Week 36 Visit, but no later than the intended Week 52 Visit.)
- At or after the Week 36 Visit, but prior to the Week 52 echocardiogram: We will do

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an exit echocardiogram when you leave the study. We will not do another echocardiogram after that.

Use of Your Leftover Blood Sample for Future Research – MGH Only

With your permission, blood samples that remain leftover after the laboratory tests will be divided into several parts and frozen in a research collection or “bank.” In the future, we may isolate DNA (your genetic, inherited material) from the cells in your blood. Your DNA and other parts of your blood sample may be used to study genes related to obesity. The results of any genetic testing will not be available to you or the doctors taking care of you.

These test results will not be entered into your medical record, and will not affect your care in any way. Your sample will be labeled with a code. Only the study doctors at MGH will be able to link your sample to your name and medical record number. This information and all of the information obtained from the samples will be kept confidential in a secured computer database. Only approved study staff will have access to this information.

Samples will be maintained in the bank until they have been completely used up. You may withdraw your sample at any time by asking the study doctor in charge of this study.

Do you agree to this? **(Please check and initial your choice)**

YES, it’s OK to use my samples for genetic research

_____ **Initials**

NO, don’t use my samples for genetic research

_____ **Initials**

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

Risks of Lorcaserin

All medications may cause side effects. There may be side effects from taking lorcaserin hydrochloride that are not yet known. The study doctor and the sponsor will tell you right away about any new side effects that occur, so that you can decide whether to stay in this study.

There is only limited information available regarding the side effects of lorcaserin in humans.

Lorcaserin may cause drowsiness. You should exercise caution and not drive, operate machinery, or engage in other activities requiring mental alertness until you know how the study drug will affect you.

In the first study with lorcaserin, up to 20 mg was associated with side effects of headache, dizziness, blurred vision and lightheadedness. Gastrointestinal effects (nausea, vomiting, and indigestion) were reported.

At a dose of 40 mg, a few subjects experienced mild euphoria (exaggerated feeling of wellbeing). One subject had symptoms of euphoria and intoxication (feeling drunk). These were followed by disorientation (feeling very confused), feelings of hot and cold, and a possible hallucination (seeing or hearing things that aren't real). You will not take more than 10 mg at a time in this study.

In the second study with lorcaserin, daily doses of up to 20 mg were taken for 14 days. The most common side effects were headache, drowsiness, lightheadedness, nausea, and vomiting. All of these symptoms tended to occur only once, were mild or moderate in intensity, and lasted for hours rather than days.

In the third study with lorcaserin, doses of 1, 5, and 15 mg once a day were taken for 4 weeks. The most common side effects were headache, drowsiness, lightheadedness, and nausea.

In the fourth study with lorcaserin, subjects took doses of 10 mg once a day, 15 mg once a day, or 10 mg twice a day for 12 weeks. The most common side effects reported were headache, lightheadedness, dry mouth, fatigue, diarrhea, nausea, and vomiting. One woman developed depression after taking lorcaserin 10 mg twice a day for about 6 weeks. Another woman who had never before had a seizure experienced a seizure after taking lorcaserin 10 mg twice a day for about 6 weeks. We do not know if these events are related to taking lorcaserin.

Some predictions can be made from animal studies with lorcaserin and from human studies of other drugs similar to lorcaserin. Lorcaserin is a member of a group of drugs known as serotonin agonists. A serotonin agonist stimulates serotonin receptors, located in the part of the brain

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called the hypothalamus, which helps regulate satiety (how full you feel) and influences metabolic rate (how much food your body needs).

Potential Brain Effects

Effects on the brain were the most frequently seen side effects of lorcaserin in animals. These brain effects in animals included decreased activity, sleeplessness, and vomiting. In some animals at high doses the brain effects were severe, and led to fits (for example, seizures and convulsions). These effects in animals were related to the amount of drug given. They were seen only at high doses (much higher than doses in this study). Such effects, along with headaches and distorted thinking (hallucinations) have also been seen with other serotonin agonists (drugs similar to lorcaserin) in humans.

As with any drug that activates the serotonin system, there is a risk of developing “serotonin syndrome.” This syndrome results from excessive amounts of serotonin released in the brain. It can be fatal if not treated promptly. Please report any adverse (bad or unwanted) feelings you may have to the study staff immediately. Adverse feelings may include headaches, nausea or other occasions where you feel sick. The sponsor does not expect that lorcaserin will cause serotonin syndrome. Studies in animals appear to show that the drug does not cause an increase in serotonin in the brain. However, the effects of lorcaserin in humans are not fully known.

Potential Heart and Lung Effects

Some serotonin agents that were used to treat obesity caused heart valve changes. In a few extreme cases, these changes meant the patient had to have an operation to fix their heart valves. In addition, these same drugs may have caused a condition called "pulmonary artery hypertension (PAH)". PAH occurs when the pressure in one of the main blood vessels leading to the lungs becomes much higher than normal. PAH is a life-threatening condition, and there is no known treatment for it. These drugs are no longer given to patients for any health condition.

Changes to heart valves caused by other drugs will generally respond to treatment with medication if discovered early enough. We require subjects to have echocardiogram tests in this study to watch for these changes. In rare cases with other drugs like fenfluramine, patients have had to have an operation to repair their heart valves.

No apparent drug-related changes in heart valves have been seen in studies of lorcaserin with animals or people to date. Likewise, no apparent drug-related increases in pulmonary arterial pressure have been observed to date.

Other Potential Drug Effects

In some animals given lorcaserin, spontaneous erections of the penis were seen. These always

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settled spontaneously. This effect has not been observed in human research studies of lorcaserin to date. However, the condition could require medical treatment if it occurred and did not resolve spontaneously.

At the highest doses tested, minor changes occurred in the lungs, liver, and kidneys of animals. You will be monitored during the study for any signs/evidence of this.

Some rats given lorcaserin at very high doses for 6 months or up to a year or more developed tumors of the breast in an ongoing two year study. Breast tumors occur commonly in rats that receive certain drugs that act on the brain. This finding is thought to be limited to rats and of questionable importance for humans. Several drugs have been approved with this finding, including a sleep drug. Mice and monkeys have not developed breast tumors when given lorcaserin.

A small number of rats in this same ongoing two year study that were given very high doses of lorcaserin were found to have brain tumors. The type of brain tumor that was found occurs naturally in a small percent of rats that do not receive any drug.

There may be side effects other than those described in this consent form. We will closely monitor your health throughout the study. There will be regular checks of your vital signs [blood pressure, heart rate (how fast your heart is beating), and body temperature]. We will also do ECGs and blood and urine test. If there are any concerns about these, they will be discussed with you. Repeat tests may be necessary for your welfare and safety.

Other Possible Effects

You could also have an allergic reaction to the study drug. This could be mild, or even fatal. For your safety, you must tell your study doctor about your past and present medical events. Tell your study doctor about any allergies you have and about all medications and drugs you now take. This includes over-the-counter drugs and herbal or food supplements.

As with all medications, if you fail to follow dosage instructions, this may result in unwanted side effects and may be dangerous for your health.

There are no known risks associated with echocardiograms. You may feel a little uncomfortable lying still on your back during the test.

The most common side effects of blood drawing include mild discomfort or feeling faint. A bruise may form where the needle enters your vein. Other risks may include bleeding from and infection at the puncture site. If an infection develops, it can be treated. The total amount of

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blood to be collected for the entire study will be less than the amount you would give in donating blood (less than 2 cups).

There are no known side effects from the ECG procedure other than local skin irritation or itching. It may be necessary to shave small areas of the chest for the attachment of disposable sticky pads.

Fasting may cause dizziness, headaches, stomach discomfort, or fainting.

You must not take part in another research study while taking part in this study. If you have recently taken part in a research study, please tell the study coordinator.

Genetic testing

Genetic information that results from this study does not have medical or treatment importance at this time. However, information about taking part in a genetic study may influence insurance and/or employers regarding your health status. If you do not share information about taking part in this study with others, you will reduce these risks. We will not place information about your participation in the study or the results of study tests in your medical record.

Special Information for Women

The effects of the study drug on an unborn baby are unknown. Some drugs cause birth defects. These may include physical defects, mental problems, and early birth. Other unknown birth defects may occur. Because of this, you must not enter this study if you are pregnant or planning on becoming pregnant. If you think you are pregnant, you must tell the study doctor immediately.

Women who can become pregnant

Women who can become pregnant must agree to use an effective method of birth control in order to be in this study. Effective methods include, but are not limited to, the following:

- Single-barrier method (for example, diaphragm, condom, spermicidal jelly, or foam)
- Intrauterine device (IUD)
- Surgical sterility. If you had surgery to remove your ovaries and/or uterus (womb) at least 6 months ago, or a tubal ligation (tubes tied) at least 3 months ago, this may qualify.
- Hormonal contraceptives (birth control pills, implants, and patches)
- Postmenopausal status (defined as at least 2 years without menstrual periods).

You must agree to use birth control while in the study and for at least 3 months after you stop taking study drug. Promising abstinence (no sexual intercourse) or having a sterile partner at the

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start of the study are not acceptable methods of birth control for this study. Rather, you must agree to use one of the approved methods of birth control should you become sexually active or have a non-sterile partner. If you are unwilling, or your partner is unwilling, to use an acceptable method of birth control during and for at least 3 months after you stop taking study drug, you will not be allowed to enter the study.

If you have had a tubal ligation, please initial that you have read and understand these requirements for entering the study.

Not Applicable or _____ **Initials**

All women will have a serum (by blood) pregnancy test at the Screening Visit. A urine pregnancy test will be done on Day 1, before giving you any study tablets. The tests must be negative in order to enter or continue in the study.

In addition, we will test your urine for pregnancy at each visit, and will do a blood pregnancy test at Week 52 (or whenever you leave the study) to be sure that you are not pregnant when you leave the study. If at any time during the study you believe you may be pregnant, you must tell your study doctor immediately. You cannot continue in the study if you become pregnant.

Even when using birth control, there is a small risk you could become pregnant. You must be tested during the study to see if you are pregnant. The test **does not prevent** you from becoming pregnant. It is not 100% (certain) proof that you are not pregnant. It will only prove pregnancy a week or 2 **after** you are already pregnant. If you stop taking the study drugs when your pregnancy is confirmed, you cannot be sure your baby has not been hurt. If you become pregnant during the study, the study doctor will advise you on proper care. All financial aspects of your pregnancy are your responsibility.

Staff members have talked with you about what method you are using not to become pregnant. They have also talked with you about not becoming pregnant during this study.

If you become pregnant during the study, you will be taken out of the study without your consent. We will also request copies of your medical records related to your pregnancy for up to 5 years after birth. Additional laboratory tests may be required. *Please initial that you have read this paragraph.*

_____ **Initials**

Except for complete abstinence (no sexual intercourse), no method of birth control is 100% certain to prevent pregnancy. However, abstinence is not an acceptable method of birth control for this study. Although the risk of becoming pregnant is low with many methods, unplanned

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pregnancies occur with all birth control methods. Most occur because of improper use of birth control.

If you miss a menstrual period or are even a few days late or think you might be pregnant at any time during this study, contact your study doctor or nurse immediately.

Also, **CALL THE STUDY DOCTOR OR NURSE IMMEDIATELY (telephone number: 617-726-4400) if:**

- you need to stop or change your birth control method,
- you are taking birth control pills and begin taking antibiotics, or
- you have a change in your menstrual cycle (timing of your period) while you are in the study, or for 3 months after you finish the study.

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I confirm that I will use only the forms of birth control allowed in this study. I have read and understand the above information. I willingly sign this consent. I will receive a signed and dated copy. All questions that I have asked have been answered to my satisfaction. I do not give up any of my legal rights by signing this form.

SIGNATURE OF PATIENT	DATE	TIME	PRINTED NAME
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SIGNATURE OF PERSON ADMINISTERING CONSENT	DATE	PRINTED NAME
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Special Information for Men

To take part in this study, you must agree that you and your partner will use an effective means of birth control, as described above. You must use it during the study and for at least 3 months after you stop taking study drug. If you are unwilling, or your partner is unwilling, we cannot allow you to enter the study.

Please initial that you have read this information and agree to the use of an acceptable method of contraception.

Not Applicable or _____ **Initials**

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

You may not receive any personal medical benefit. There are health benefits to losing weight, but you are not guaranteed to lose weight during this study. The only direct benefit to you will be the evaluation and review of your health by the examining study doctor.

You may receive some benefit from taking part in the Arena[®] Healthy Lifestyles Program, a weight management program designed specifically for this study. The knowledge and materials you gain from this program may benefit you; even after your study participation is complete.

In addition, the information learned from this study as a result of your participation may benefit others in the future.

What other treatments or procedures are available for my condition?

This is a research study and is not the same as treatment or therapy. If you do not qualify for the study, or choose not to take part in this study, your doctor can discuss other treatments with you. These may include diet and exercise programs, other drugs (including sibutramine, orlistat and phentermine), a combination, or even surgery for some cases.

Can I still get medical care within Partners if I don't take part in this research study, or if I stop taking part?

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

Taking part in this research study is up to you. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. We will tell you if we learn new information that could make you change your mind about taking part in this research study.

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

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

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

You will receive a total of \$700.00 for completing the study. In addition, we will also reimburse you for parking and transportation expenses. The maximum compensation is not negotiable. You will be compensated for completing parts of the study according to the following schedule:

When you complete all visits through...	You will receive...
Week 12	\$100
Week 24	\$100
Week 36	\$100
Week 56	\$400
Total	\$700

If drug screen results are positive or if you have lab abnormalities that prevent you from enrolling in the study, you will only receive compensation for parking and transportation.

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

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

The costs of the study drug and all tests and procedures will be paid by study funds.

What happens if I am injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them.

If you are injured or become ill, you must tell the study doctor at once. If you are injured as a result of the study drug or study procedures, you should seek medical attention with a medical provider of your choice. The Sponsor will cover the medical expenses of seeing an accredited/certified provider for reasonable treatment of an injury resulting from your taking part in this study. Medical expenses include costs that are not covered by your health insurance

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policy, by a government program, or by any other third party. This does not include care for any illness not coming from the research study

There are no plans to pay you for lost wages, discomfort, or disability because of injury or illness.

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

Giving you care does not mean that Partners hospitals or researchers are at fault, or that there was any wrongdoing. There are no plans for Partners to pay you or give you other compensation for the injury. However, you are not giving up any of your legal rights by signing this form.

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

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

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

Lee Kaplan, MD, PhD is the person in charge of this research study. You can call him at **617-726-4400** during regular office hours. For urgent matters, he can be paged through the hospital operator 617-726-2000 nights and weekends.

You can also reach Carolyn Robinson, the study coordinator, at **617-724-9616** during regular office hours or by e-mail at crobinson12@partners.org with questions about this research study or about the scheduling of appointments or study visits.

If you want to speak with someone **not** directly involved in this research study, please contact the Partners Human Research Committee office. You can call them at 617-424-4100.

You can talk to them about:

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- Your rights as a research subject
- Your concerns about the research
- A complaint about the research

Also, if you feel pressured to take part in this research study, or to continue with it, they want to know and can help.

If I take part in this research study, how will you protect my privacy?

Federal law requires Partners (Partners HealthCare System and its hospitals, health care providers and researchers) to protect the privacy of health information that identifies you. This information is called Protected Health Information. In the rest of this section, we refer to this simply as “health information.”

If you decide to take part in this research study, your health information may be used within Partners and may be shared with others outside of Partners, as explained below.

We have marked with a how we plan to use and share your health information. If a box is not checked , it means that type of use or sharing is not planned for in this research study.

We will also give you the **Partners Notice for Use and Sharing of Protected Health Information**. The Notice gives more details about how we use and share your health information.

▪ **Health Information About You That Might be Used or Shared During This Research**

- Information from your hospital or office health records within Partners or elsewhere, that may be reasonably related to the conduct and oversight of the research study. If health information is needed from your doctors or hospitals outside Partners, you will be asked to give permission for these records to be sent to researchers within Partners.
- New health information from tests, procedures, visits, interviews, or forms filled out as part of this research study

▪ **Why Health Information About You Might be Used or Shared with Others**

The reasons we might use or share your health information are:

- To do the research described above

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- To make sure we do the research according to certain standards - standards set by ethics and law, and by quality groups
- For public health and safety - for example, if we learn new health information that could mean harm to you or others, we may need to report this to a public health or a public safety authority
- For treatment, payment, or health care operations

▪ People and Groups That May Use or Share Your Health Information

1. People or groups within Partners

- Researchers and the staff involved in this research study
- The Partners review board that oversees the research
- Staff within Partners who need the information to do their jobs (such as billing, or for overseeing quality of care or research)

2. People or groups outside Partners

- People or groups that we hire to do certain work for us, such as data storage companies, our insurers, or our lawyers
- Federal and state agencies (such as the U.S. Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health, and/or the Office for Human Research Protections) and other U.S. or foreign government bodies, if required by law or involved in overseeing the research
- Organizations that make sure hospital standards are met
- The sponsor(s) of the research study, and people or groups it hires to help perform this research study
- Other researchers and medical centers that are part of this research study
- A group that oversees the data (study information) and safety of this research study
- Other:

Some people or groups who get your health information might not have to follow the same privacy rules that we follow. We share your health information only when we must, and we ask anyone who receives it from us to protect your privacy. However, once your information is shared outside Partners, we cannot promise that it will remain private.

▪ Time Period During Which Your Health Information Might be Used or Shared With Others

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- Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your health information.

▪ **Your Privacy Rights**

- You have the right **not** to sign this form permitting us to use and share your health information for research. If you don't sign this form, you can't take part in this research study. This is because we need to use the health information of everyone who takes part in this research study.
- You have the right to withdraw your permission for us to use or share your health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others. This includes information used or shared to carry out the research study or to be sure the research is safe and of high quality.

If you withdraw your permission, you cannot continue to take part in this research study.

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

▪ **If Research Results Are Published or Used to Teach Others**

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

Consent/Assent to take part in this research study, and authorization to use or share your health information for research

Statement of Subject or Person Giving Consent/Assent

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

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If you understand the information we have given you, and would like to take part in this research study, and also agree to allow your health information to be used and shared as described above, then please sign below:

Signature of Subject:

Adults or Minors, ages 14-17

Date/Time

OR

If you understand the information we have given you, and would like to give your permission for your child/the person you are authorized to represent to take part in this research study, and also agree to allow his/her health information to be used and shared as described above, then please sign below:

Signature of Parent(s)/Guardian or Authorized Representative:

Parent(s)/Guardian of Minor

Date/Time

OR

Court-appointed Guardian or Health Care Proxy

Date/Time

OR

Family Member/Next-of-Kin

Date/Time

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Relationship to Subject: _____

Signature of a Witness:

Witness (when required by the PHRC or sponsor)

Date/Time

Statement of Study Doctor or Person Obtaining Consent

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

Study Doctor or Person Obtaining Consent

Date/Time

In certain situations, the Partners Human Research Committee (PHRC) will require that a subject advocate also be involved in the consent process. The subject advocate is a person who looks out for the interests of the study subject. This person is not directly involved in carrying out the research. By signing below, the subject advocate represents (or “says”) that the subject has given meaningful consent to take part in the research study.

Statement of Subject Advocate Witnessing the Consent Process

- I represent that the subject or authorized individual signing above has given meaningful consent.

Subject Advocate (when required by the PHRC or sponsor)

Date/Time

Consent Form Version Date: