

**INFORMED CONSENT FORM TO TAKE PART IN A CLINICAL RESEARCH STUDY  
AND  
AUTHORIZATION TO DISCLOSE HEALTH INFORMATION**

**Sponsor/Study Title:**

**The Medicines Company/ “An Open-Label Study Evaluating the Effects of a Single Oritavancin Infusion on Cytochrome P450 (CYP) 1A2, CYP2C9, CYP2C19, CYP2D6, CYP3A, *N*-Acetyltransferase-2, and Xanthine Oxidase Activities in Healthy Adults using the Cooperstown 5 + 1 Cocktail”**

**Protocol Number:**

**MDCO-ORI-12-03**

**Principal Investigator/Study Physician:**

**Carlos Sanabria, MD**

**Telephone:**

**800.597.4507 (Recruitment Department)  
855.622.8100 (24-hour urgent question/care)**

**Additional Contact(s):**



**Address:**

**Spaulding Clinical Research, LLC  
525 S Silverbrook Dr.  
West Bend, WI 53095**

**SUBJECT SCREENING # \_\_\_\_\_**

Please read this form carefully. Take time to ask the study physician or study staff as many questions about the study as you would like. The study physician or study staff can explain words or information that you do not understand. Reading this form and talking to the study physician or study staff may help you decide whether to take part or not. If you decide to take part in this study, you must sign your name at the end of this form. You cannot take part in this research study until you sign this form.

**WHAT IS A VOLUNTEER INFORMED CONSENT?**

You are being asked to take part in a research study of an experimental drug Oritavancin in an intravenous (IV) (in your vein) formulation that has not been approved by the U.S. Food and Drug Administration (FDA), to find out if the drug is safe. Before you can make a decision to take part, you should understand the possible benefits and risks associated with this study. This process is known as informed consent and means that you will:

- Receive detailed information about this research study.
- Have a chance to ask and receive answers to any questions you may have.
- Be asked to read and sign this informed consent, once you understand the study and wish to take part.
- Be given a signed and dated copy of this informed consent to keep.

Carlos Sanabria, MD

*Chesapeake IRB Approved Version  
DD/MMM/YYYY*

*Subject's Initials \_\_\_\_\_*

Taking part in this study is entirely voluntary.

### **WHY IS THIS DRUG BEING STUDIED?**

This is a clinical research study. This study is sponsored by a pharmaceutical company named The Medicines Company based in New Jersey, US.

If you agree to participate in this study, you will be given Oritavancin and the Cooperstown 5 + 1 Cocktail.

Oritavancin is an investigational drug for the treatment of acute bacterial skin and skin structure infections. Examples include wound infections, cellulitis, and abscesses. These infections commonly require quick treatment to minimize tissue damage, prevent further spread of the infection, and aide in the recovery of the patient. Oritavancin is an antibiotic designed to treat bacterial infections that other antibiotics cannot treat, such as MRSA (methicillin-resistant *Staphylococcus aureus*). The dosage form of Oritavancin under investigation is an intravenous (IV) (administered into your vein) formulation.

The Cooperstown 5 + 1 cocktail is a combination of the following 6 medicines: Caffeine, Warfarin, Vitamin K, Omeprazole, Dextromethorphan and Midazolam. Caffeine is a central nervous system stimulant that increases alertness. Warfarin is commonly referred to as a “blood thinner.” It decreases the blood’s ability to form a clot. Vitamin K increases the ability of blood to clot. Omeprazole is a medicine classified as a proton pump inhibitor. It is used for decreasing the acidity of the stomach. Dextromethorphan is a cough suppressant. Midazolam is classified as a benzodiazepine; it causes mild sedation and drowsiness.

The dosage form of Oritavancin under investigation is an intravenous (IV) (in your vein) formulation. The dosage form of the Cooperstown 5 + 1 cocktail is 6 oral doses (tablets and/or liquid by mouth).

The goal of this study is to evaluate the effects of Oritavancin on certain cytochromes with administration of the Cooperstown 5 + 1 cocktail. Cytochromes are specific enzymes located in your liver that participate in drug metabolism. You will be given the Cooperstown 5 + 1 cocktail twice and Oritavancin once during the study. The Cooperstown Cocktail is often referred to as the “probe drug”.

### **WHO IS BEING ASKED TO TAKE PART IN THIS STUDY?**

Approximately 16 healthy male and female adult subjects, who meet the requirements following a screening visit, will be enrolled in the study.

You have been asked to take part in this study because you are in general good health, are 18-45 years of age, are a non-smoker, have no history of heart or liver disease, no history of allergies, and have not participated in another research study for an experimental drug (or a medical device) within 30 days of the first dose of study drug.

### **HOW MUCH TIME IS REQUIRED TO TAKE PART IN THE STUDY?**

If you decide to take part in the study, you will be asked to attend a screening visit. If you pass the screening visit, you will return to the clinic for one period of confinement lasting 10 days/ 9 nights at the study site. When you have completed the inpatient period you will be asked to return to the clinic for 3 follow-up visits. The first follow-up visit will be approximately 8 days (Day 8) following study drug administration (3 days after inpatient discharge). The second follow-up visit will be approximately 16 days (Day 16) following study drug administration (11 days after inpatient discharge). The third follow-up visit will be approximately 28 days (Day 28) following study drug administration (23 days after

inpatient discharge). By the end of this study you will have spent 10 days and 9 nights in the clinic and completed 3 follow-up visits.

The duration of your participation in the study from screening to final follow-up will be up to 60 days.

### **INFORMATION FOR FEMALE VOLUNTEERS**

You should not screen for this study if:

- There is any possibility that you may become, or are pregnant,
- You have given birth in the last 3 months, or
- You are breast feeding, or
- You plan to get pregnant in the next 3 months

You may screen for this study if:

- You are surgically sterile, meaning you have had a hysterectomy (uterus removed) or bilateral oophorectomy (ovaries removed), or
- You are using an adequate method of non-hormonal contraception to avoid pregnancy throughout the study and for 3 months after last study drug administration.
- You are of post-menopausal age and have not had a menstrual period for 2 years, confirmed with hormone level at screening.

Adequate methods of contraception include use one of the following categories.

- Condom (female or male), with spermicide
- Diaphragm, with spermicide
- Non-hormonal Intrauterine device (IUD),

The use of spermicide alone and condom alone are not acceptable methods of contraception.

Except for continuous abstinence (no sexual intercourse with a male partner), no method of birth control can be considered 100% reliable in preventing pregnancy. Although the risk of becoming pregnant is low with many methods, unplanned pregnancies may occur with all birth control methods. Most occur because of improper or irregular use of the birth control method. If you are usually not sexually active but become sexually active, you must follow the advice documented above regarding contraceptive methods.

All females enrolled in this study will have a pregnancy test performed at screening, before admission (Day -5), and at last follow-up visit (Day 28).

Please be aware that a pregnancy test may not be positive until 12 days after conception (fertilization of the egg by sperm). Therefore, if you do not follow the study birth control requirements and/or your birth control method has failed, you will not be able to count on a negative test to confirm that you are not pregnant.

If you know that you have not followed the study birth control requirements outlined above, then you must immediately inform us. You must not take any dose of the study drug if you have not followed these requirements.

## INFORMATION FOR MALE VOLUNTEERS

Male subjects must ensure that two acceptable methods of contraception are used for the entire duration of the study, up to the study follow-up visit, if applicable.

The effect of the study drug on male sperm is unknown. In rare cases, drugs may damage sperm in ways that affect a child that is fathered. Affected sperm may be present in the semen for about 3 months. Therefore, it is recommended to avoid fathering a child for 90 days after the last dose of the study drug.

Periodic abstinence and withdrawal are not acceptable methods of contraception.

## HOW WILL YOU KNOW IF YOU ARE ELIGIBLE TO TAKE PART?

You will need to fast for at least 10 hours prior to your arrival at Spaulding Clinical Research, LLC. for your screening visit, meaning you should not eat any food and should only have water to drink.

At the beginning of the Screening visit, Informed Consent will be obtained.

**Before starting the study**, the following screening procedures will be performed:

- A complete medical history and physical examination (including height and weight measurements for Body Mass Index (BMI, a way to tell if your weight is proportional to your height).
- Assessment of blood pressure, respiratory rate, heart rate, pulse oximetry, and oral temperature.
- A complete history of relevant allergies or drug sensitivities and previous medications.
- An electrocardiogram (ECG), (a painless recording of the electrical activity of your heart).
- You will be asked if you have taken any medication recently.
- You will be asked if you have been feeling ill recently.
- Clinical laboratory tests (urine and blood samples), including screening for drugs, alcohol, and pregnancy tests (all female subjects), hormone panel (post-menopausal female subjects only), International Normalized Ratio (INR – a test to evaluate the body's ability to clot blood), and testing for HIV, hepatitis B and C. Positive results of HIV or hepatitis tests will be reported to local health authorities as required by state law.

If you meet the “entry criteria” of the study, according to the study physician, you will be tested again when you are admitted to Spaulding Clinical Research, LLC. You will have the entry criteria reviewed again to ensure that you still are eligible for the study.

## HOW WILL THE STUDY BE DONE?

Sixteen healthy adult subjects, both male and female will be enrolled in this study. Once the study physician determines that you are eligible to participate, you will be enrolled into the study. Because this is an open-label study, you, the study staff, and study physician will all know what treatments you will be receiving. The study will consist of one treatment period of 10 days/ 9 nights. You will not be allowed to choose when you receive the doses. All subjects will receive the treatments described in the next section, “What Tests And Procedures Will Be Used In the Study?”

## WHAT TESTS AND PROCEDURES WILL BE USED IN THE STUDY?

### Day -5 Admission

Upon admission to Spaulding Clinical Research, LLC., you will be given an identity band to wear throughout your entire stay in the unit.

You will need to fast for at least 10 hours prior to your arrival meaning you should not eat any food and should only have water to drink.

The following activities will be performed at this visit:

- Meals (lunch, dinner, snack)
- Medical history updates.
- Physical examination.
- Weight.
- Safety ECG collection.
- Vital sign collection (blood pressure, pulse rate, respiration rate, pulse oximetry, and oral temperature).
- Clinical laboratory tests (urine and blood samples), including screening for drugs, alcohol, and pregnancy tests (all female subjects).
- A pharmacogenomic (gene testing) blood sample will be drawn (Day -5 only). This will be one tube of blood (4ml total) that will be collected for potential future testing. These tests help to determine if your genetic make-up slows down or speeds up the way your body metabolizes (gets rid of) medications.
  - Pharmacogenetics looks at how genes influence the different responses people have to the same drug. Genes contain the instructions for making all living things and are contained in DNA. Most DNA is the same among human beings, but the small variations we all have in our DNA causes differences in people, such as different sizes and hair color. These kinds of differences may also explain why different people have different responses to the same drug.
  - This pharmacogenomic study will not identify information that could be used to change your medical care, make or change your diagnosis, or determine your risk of diseases. Any personal health information about you, including any genetic information, will be kept confidential.
- You will be asked for details of any medication taken since the screening or previous visit.
- You will be asked if you have been ill since the screening or previous visit.
- You will be asked if you complied with study restrictions.
- Inclusion/Exclusion assessment and preparation for randomization.

The results from these tests will help the study staff determine whether you are still eligible to enter the study. None of these tests are investigational and are commonly performed during routine medical care.

### Day -4

- Administration of Cooperstown Cocktail 5 + 1 consists of the following 6 oral doses (tablets and/or liquid by mouth): 2 mg/kg caffeine (calculated with Day -5 weight); 10 mg warfarin; 10 mg vitamin K; 40 mg omeprazole; 30 mg dextromethorphan and 0.075mg/kg midazolam (calculated with Day -5 weight)
  - midazolam will be dosed three hours prior to the remainder of the Cooperstown Cocktail
- Safety ECG collections

- Vital sign collections
- Pharmacokinetic (PK) blood and urine (12 hour urine collection) sampling (blood/urine samples for determination of probe drug levels). Pharmacokinetics looks at how your body:
  - Takes the drug into your bloodstream.
  - Delivers the drug through the blood.
  - Breaks down or processes the drug.
  - Removes the drug.
- Adverse event assessment (check for side effects) and changes in concomitant medications (medicines you are currently taking).
- Meals (lunch, dinner and a small snack).

**Days -3, -2, & -1**

- Adverse event assessment and changes in concomitant medications
- Vital sign collection
- Pharmacokinetic (PK) blood sampling for probe drug levels.
- Meals (breakfast, lunch, dinner and a small snack).

**Study Treatment (Day 1)**

- Adverse event assessment and changes in concomitant medications
- Clinical laboratory tests (urine and blood samples)
- Safety ECG collections.
- Vital sign collections
- Administration of Oritavancin IV for 3 hours, along with assessment of local tolerability at the site of administration.
- Administration of Cooperstown 5 + 1 cocktail after Oritavancin 3 hour infusion is complete.
  - midazolam will be dosed three hours prior to the remainder of the Cooperstown Cocktail (at approximately same time as IV Oritavancin is started).
- Pharmacokinetic (PK) blood for study drug and probe drug and urine (12 hour urine collection) sampling for probe drug.
- Physical Exam
- Meals (lunch, dinner, and a small snack).

**Days 2, 3 & 4**

- Adverse event assessment and changes in concomitant medications.
- Pharmacokinetic (PK) blood sampling for both probe drug and study drug.
- Vital sign collections
- Meals (breakfast, lunch, dinner, and a small snack)

**Day 5 (or Early Termination)**

- Adverse event assessment and changes in concomitant medications.
- Pharmacokinetic (PK) blood sampling for probe drug.
- Clinical laboratory tests (urine and blood samples)
- Physical examination.
- Vital sign collection.
- Safety ECG collection.

- Breakfast.

You will be discharged from the unit following completion of the 96 hour PK sampling and all other procedures.

#### **Follow-Up Day 8 and Day 16**

- Adverse event assessment and changes in concomitant medications.
- Pharmacokinetic (PK) blood sampling for study drug.

#### **Follow-Up Day 28 (Study Completion)**

- Adverse event assessment and changes in concomitant medications.
- Vital sign collection.
- Safety ECG collection.
- Clinical laboratory tests (urine and blood samples, FASTING) and pregnancy tests (all female subjects).
- Physical examination.

### **INFORMATION OBTAINED DURING THE STUDY**

#### **Blood Sampling**

Blood samples will be collected for measurement of levels of Oritavancin at approximately the following times:

- Day 1 at pre-dose and at 1.5, 3, 4, 6, 8, 12,
- Days 2, 3, 4, 8, and 16 at 24, 48, 72, 192 and 384 hours after the start of the dose of oritavancin for a total of approximately 12 blood collections for determining study drug levels.

Blood samples will be collected for measurement of levels of Cooperstown 5 + 1 Cocktail at approximately the following times:

- Day-4 and Day 1 at pre-dose, and at 5 minutes, 30 minutes, and 1, 2, 3, 4, 5, 6, 8, 12 after dosing,
- Days -3, -2, -1 and Days 2, 3, 4, and 5 at 24, 36, 48, 72, and 96 hours after dosing.  
This is a total of approximately 32 blood collections for determining warfarin, omeprazole, and midazolam levels.

You will have numerous blood samples drawn during the entire study for study drug levels as shown above, and 5 safety laboratory draws throughout the study. The blood samples may be taken by individual needle sticks into one of your arm veins, or, if necessary, by an indwelling catheter (a thin plastic tube placed in a vein in your arm). The total amount of blood taken for the entire study will be approximately 359 mL: 15 mL for screening, 300 mL for the determination of Oritavancin and Cooperstown 5 + 1 cocktail concentrations, 4 mL for pharmacogenomic testing, and 40 mL for clinical laboratory tests) or about 1 and 1/2 cups for the entire study.

One of the samples collected may undergo pharmacogenomic testing. Pharmacogenomics is the study of differences in how our bodies respond to or handle medicines. This research will look at genetic differences to better understand why people react differently when they get the same medicine. Any personal health information about you, including any genetic information, will be kept confidential.

### **Urine Sampling**

Urine samples for urinalysis, drugs, alcohol, and/or pregnancy will be collected at screening, on Day -5 (Check-In), Day 1, Day 5 (Check-Out), and on final Follow-up Visit on Day 28. As part of the PK (pharmacokinetic) measurement of the Cooperstown Cocktail, you will also be collecting all of your urine from just prior to dosing on Day -4, until 12 hours following dosing on Day -4. This same urine collection will be repeated on Day 1.

You will be given instructions on how to collect the urine during this 12-hour period. Spaulding Clinical will be providing special containers to collect this urine. Your study schedule will include specific times to start and stop this collection.

This urine sampling requires that **during the times designated** above and on your schedule, you will not urinate without collection. You will report to the central laboratory as designated as your start and stop times, and also any other time that you feel the need to void. Clinical staff will provide you with a collection device and will ensure that all urine is properly collected and stored.

### **ECG Measurements**

Safety ECG measurements will occur at your screening visit, Days -5, -4, 1, 5 and on your last Follow-Up visits (Day 28). On the dates of your safety ECG, there will be a period of time lasting approximately 20 minutes where you will need to lie very still to get precise readings of your heart's rhythm.

Some individuals may develop redness and irritation at the site of ECG electrodes placed on the chest/body. This may develop due to sensitivity to the electrodes or to our skin preparation procedure. In order to get the quality results we need, it is necessary for us lightly scrub the skin with an abrasive pad to remove any skin impedance such as oil, dead skin cells and lotions. We may trace each electrode site with a permanent marker to assure electrodes are placed in the same place on the body for each ECG event to maintain quality and consistent results. This tracing may occur as often as once a day during confinement.

### **WHAT ARE YOUR RESTRICTIONS DURING THE STUDY?**

You will need to avoid the following while taking part in this study, and most importantly from the time of your screening visit until you check in:

- Strenuous exercise, caffeine or theobromine-containing products (e.g., coffee, tea, energy drinks, cola or chocolate) consumption, broccoli, brussels sprouts, and charcoal grilled meats for 48 hours prior to study drug administration and for the duration until Follow-Up visit on Day 28 has been completed.
- Alcohol intake within 1 month prior to Screening and until Follow-Up visit on Day 28 has been completed.
- Orange/grapefruit, including Seville oranges, (and containing products, such as juices) are not allowed from 48 hours prior to study drug administration and until Follow-Up visit on Day 28 has been completed.
- Using non-prescription medications for 30 days prior to Check-In (Day -5) or prescription medications for 3 months prior to Screening, until the last pharmacokinetic sample has been drawn.
- Male and female subjects must adhere to contraception methods as previously stated.

You will receive a diet that does not contain any alcohol or caffeine. You must eat all of each meal that is served to you and eat at a reasonable pace.

You may eat only meals and snacks that are provided to you during periods of your stay.

### **ARE THERE RISKS TO YOU IF YOU ARE IN THIS STUDY?**

Risks are possible side effects of the study drug, the probe drugs, and those of taking blood and other medical procedures:

#### Known Risks

##### **For Oritavancin (study drug):**

The most common side effects (experienced by more than 1 in 100 patients but less than in 1 in 10 patients) possibly related to oritavancin include:

- Insomnia – difficulty falling or staying asleep
- Headache or dizziness
- Phlebitis - Pain and irritation around the vein, particularly at the site of infusion. In some cases, the phlebitis was considered painful and did not go away for several weeks. In other cases, the phlebitis took longer to go away.
- Nausea
- Itching

Side effects that are uncommon (experienced by fewer than 1 out of every 100 patients, but more than 1 out of every 1000 patients) included constipation, diarrhea, vomiting, rash, temporary changes in laboratory tests that look at the health of your liver and your kidney, increased sweating/night sweats, chills, tiredness or excessive sleep, increase or decrease in cells that help fight infections, fever, anxiety, high and/or low blood pressure, abdominal pain, abnormal taste, heart beating too fast, too slow, or irregularly, flushing, dry mouth, redness of skin, tingling, fainting, red spots or bumps on the skin, hives, sudden kidney failure, stomach pain, muscle spasms, pain in extremities such as your hands and feet, cardiac arrest, infections of the bone or blood (sepsis/septic shock), and allergic reactions.

Side effects that are rare (experienced by fewer than 1 out of every 1000 patients) include a decrease in the number of cells that help your blood clot, passing gas, sour stomach, skin infections (not related to your original infection) including abscess and cellulitis, Candida pneumonia, Candida sepsis, low blood volume, and changed mental status. It is unclear if these side effects which occurred less than 1% of the time were related to study drug.

##### **For Warfarin:**

- The most common side effect is bleeding. Bleeding can occur at any site including but not limited to nose, mouth, vagina, rectum, at the needle injection site, in the eye or inside the brain, bleeding can potentially be serious.
- Easy bruising, purple or red pinpoint spots under your skin,
- Blood in your urine, black or bloody stools, coughing up blood or vomit that looks like coffee grounds;
- Pain, swelling, hot or cold feeling,
- Sudden and severe leg or foot pain, foot ulcer, purple toes or fingers,
- Sudden headache, dizziness, or weakness,
- Pale skin, feeling light-headed or short of breath, rapid heart rate, trouble concentrating,
- Pain in your stomach, back, or sides,

- Urinating less than usual,
- Numbness or muscle weakness,
- The development of large or small blood clots or emboli that may block blood vessels,
- Vasculitis (diseases that causes inflammation of the blood vessels),
- Alopecia (hair loss)
- Changes in liver enzyme levels indicating liver damage
- Jaundice (yellowing of the skin or eyes)
- Dark urine, pancreatitis
- Nausea,
- Vomiting,
- Diarrhea,
- Skin disorders including rash, dermatitis, itching,
- Chills.

**For Caffeine:**

- Insomnia (cannot fall in sleep or wake up easily),
- Nervousness,
- Restlessness,
- Confusion or other psychotic symptoms
- Stomach irritation,
- Nausea,
- Vomiting,
- Increased heart rate and respiration
- Increased in blood pressure

**For Vitamin K:**

- Temporary redness of the face and neck,
- Temporary change in taste sensation,
- Dizziness,
- Allergic reaction.

**For Omeprazole:**

- Headache,
- Abdominal pain,
- Diarrhea
- Nausea
- Vomiting
- Flatulence
- Acid regurgitation (acid reflux)
- Constipation
- Dizziness
- Allergic reaction
- Seizure (convulsions)

**For Dextromethorphan:**

- Drowsiness,
- Nervousness,
- Restless feeling

- Dizziness,
- Nausea,
- Vomiting.

**For Midazolam:**

- Nausea
- Vomiting
- Hiccups
- Drowsiness
- Dizziness
- Short-term memory loss
- Respiratory depression/arrest (decreased and/or stopping of breathing)
- Restlessness
- Aggressiveness
- Slow in heart beats,
- Changes in heart rhythm
- Changes in blood pressure.

Problems or side effects that are not now known or rare side effects that are not listed above could also occur. You will be given any new information that may affect your willingness to start or continue in the study.

The tests done at each visit are standard medical tests. The most unpleasant is often having blood samples taken. The risks of taking blood may include:

- Fainting
- Pain
- Bruising
- Hematoma (development of a collection of blood under the skin)
- Rarely, there may be a small blood clot or infection at the site of the needle puncture

The blood pressure cuff may also cause discomfort or bruising to the upper arm.

In rare instances where a nurse, a physician, or a technician, sustains an exposure to your blood, tissue or body fluids by needle stick, cut or splash to mucosa or damaged skin, it may be necessary to test your blood, tissue, or body fluid sample for certain viral infections including Hepatitis B and C and HIV on the sample already available. This is to enable that person to receive appropriate counseling, monitoring and treatment if necessary. In this instance the study physician or designee will offer you the information relevant to your health and advise you on the next steps. Confidentiality of your data will be respected at all times according to the state law.

**Unknown Risks**

As with any drug, it is possible that you could experience an allergic reaction to the study drug used in this study. Sometimes the allergic reactions can be serious or life threatening. Symptoms of any allergic reaction can include:

- Rash
- Hives
- Itching
- Difficulty breathing or wheezing

- Closing of the throat
- Blistering of the skin, mouth, eyes and genitals
- Swelling of the lips, tongue or face
- Rarely, death.

**If you think you are having a severe allergic reaction, while outside the study center call 9-1-1 and seek medical attention immediately.**

It is very important that you tell the study physician and the study staff about any side effects that you might experience.

You may experience side effects or discomforts that are not listed on this form. Tell your study physician or study staff immediately if you have any problems. Your safety will be closely monitored during the course of the study.

### **For ECG Monitoring**

It is possible to be sensitive to the adhesives used on the electrodes that are applied to your chest when having an ECG performed. If this is the case, you could develop a temporary redness or irritation of the skin where the electrodes were applied.

### **HIV Testing**

The risks of HIV testing include psychological and social risks. A positive test can lead to restrictions in freedom of travel to some countries and possible prejudices in job employment, insurance eligibility, housing and other forms of discrimination. Positive HIV test results must be reported to health authorities under state law.

### **Reproductive Risks**

The effects of the test drug on human pregnancy and the unborn child (fetus) are unknown. Therefore, it is very important that you do everything within your power not to become pregnant, or father a child during this study and for 90 days following the last dose. Please ensure that you follow the study birth control requirements outlined in the sections regarding information for male and female volunteers above.

If you become pregnant during the course of the study, you will be withdrawn from the study. Neither Spaulding Clinical Research, LLC. nor the sponsor will be responsible for the cost of any obstetric or related care, or for your child's care. The sponsor will request access to both you and your child's medical records for a minimum of 8 weeks following delivery. By signing this consent, you are agreeing to provide this information including the outcome of any pregnancy that occurs during this study.

### **Genetic Testing**

There is risk associated with the loss of privacy or confidentiality. For example, if your identifiable genetic or health information were disclosed to unauthorized persons, there is the possible risk of discrimination by employers or insurance providers.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans and most employers to discriminate against you based on your genetic information.

This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that the sponsor will get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that the sponsor will get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies and group health plans and all employers with 15 or more people must follow this law.

Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance or long-term care insurance.

## **NEW FINDINGS**

Your study physician 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 the study. You may contact the study physician at any time after your participation ends to find out if any new information about this study has become available.

## **WHAT IS THE ALTERNATIVE TO BEING IN THE STUDY?**

Since this is a study involving healthy volunteers, your alternative is not to take part.

## **WILL YOU BENEFIT FROM TAKING PART IN THE STUDY?**

You will not receive direct medical benefit from receiving the study drug. You may receive information about your health from the physical examination, and blood and urine tests as they apply to this research project.

Just by taking part in this research study, you may be helping future patients by providing important information about the study drug and by contributing to medical knowledge.

## **WHO IS PAYING FOR THIS STUDY?**

A pharmaceutical company called The Medicines Company is the Sponsor of the study. The Medicines Company is a company that creates and makes medicines.

The Medicines Company pays the site, Spaulding Clinical Research, LLC (which employs the study physician) to run this study.

The study drug and all tests, procedures and visits required by the study are provided at no cost to you. The sponsor, The Medicines Company, pays for them.

Information about this study is confidential. This information belongs to The Medicines Company. We ask that you keep it private. You can discuss this information in private with your physician or family to talk about your healthcare or to decide about taking part in this study.

## WILL YOU BE PAID FOR BEING IN THIS STUDY?

Compensation for screening is as follows:

- \$50.00 for your time, travel expenses, and inconvenience during the screening process, even if you do not qualify for the study. The \$50.00 will be paid to you after final review of the screening results.
- If the results of the drug and alcohol tests are positive, you will not receive any compensation.

Compensation for this study is as follows:

For subjects that complete the entire study (Day -5 to the Follow-Up visit Day 28), you will receive up to \$2,800.00 for your time, travel expenses and inconvenience. This payment will be made in 5 separate payments as follows:

- \$900.00 will be paid after all Check-Out procedures have been completed on Day 5.
- \$300.00 after outpatient visit on Day 8.
- \$300.00 after outpatient visit on Day 16.
- \$300.00 after the final Follow-Up visit on Day 28.
- The remaining \$1000.00 will be paid within 14 days of the final out-patient visit, any additional follow up procedures are completed, and all results are reviewed.
- If you withdraw from the study early, you will only be paid for the visits you completed. You will receive \$100.00 for your time, travel expenses and inconveniences for each full day that you were in-house.

**NOTE:** You may be required to return to the clinic for repeat blood test or other assessment (ECG, physical, vital signs) in between visits or after the final outpatient visit. This is considered part of the study and no additional compensation is available. Your final payment will not be released until all follow up procedures have been completed and accepted by the study physician. Once all follow up procedures have been completed and accepted by the study physician, your final payment will be released within 14 days of your final visit/assessment.

No deductions for any state or federal withholding or any other similar taxes will be made and you are solely responsible for reporting such payments on your state and federal income tax returns.

If you need to stay at Spaulding Clinical Research, LLC. for a longer period of time for safety reasons, you will be compensated at a rate proportional to the entire compensation for the study.

If you are dismissed from the study for medical reasons or if the study is temporarily or permanently halted, your compensation will be proportional to the time you spend in the study.

If you are dismissed from the study because you have not complied with the instructions of the study staff, no compensation is available. Non-compliance includes, but is not limited to, improper conduct, taking alcohol and/or any drugs (including recreational drugs), tampering with the study drug, or consuming any foods/beverages not allowed in the study.

By signing this consent, you expressly agree that you are an Independent Contractor for Spaulding Clinical Research, LLC. As an Independent Contractor, you will receive a 1099 form from Spaulding Clinical Research, LLC. The 1099 form shall document and report all payments and/or study stipends you received as an Independent Contractor for Spaulding Clinical Research, LLC.

Carlos Sanabria, MD

Chesapeake IRB Approved Version  
DD/MMM/YYYY

Subject's Initials \_\_\_\_\_

## COMPENSATION FOR INJURY

It is important that you follow carefully all the instructions given by the study physician and his/her study staff regarding this study.

If you become ill or are physically injured as a result of participation in this study, please contact the study physician right away at the telephone number listed on page one of this consent form. He/she will treat you or refer you for treatment.

The out of pocket costs (not covered by insurance) of reasonable and necessary treatment will be covered by the sponsor, The Medicines Company, if you are hurt by the study drug or a procedure that is done to you only because you are part of this study. The Medicines Company will provide for compensation and payment for medical expenses for injuries that resulted from Oritavancin or procedures that were performed as part of the study, so long as:

- you received reasonable medical care according to study procedures
- you followed instructions; and
- such injuries are not the result of the natural course of any underlying disease and/or pre-existing disease process present prior to the proper administration of Oritavancin. In no way does signing this consent form waive your legal rights nor does it relieve the investigators, Sponsor or involved institutions from their legal and professional responsibilities.

## PROTECTING THE PRIVACY OF YOUR HEALTH DATA

Unless required by law, your name will not be disclosed outside the research clinic. Your name will be available only to the following people or agencies: the study physician and study staff; and authorized representatives of the study physician; ethics committees, health authority inspectors, such as the US Food & Drug Administration and the European Medical Agency; The Medicines Company study monitors and auditors; and authorized Clinical Research Organization representatives. The above mentioned individuals will use the personal information collected as part of this study, including your medical records ("Study Information") to check that the study is conducted correctly and to ensure the accuracy of the study information. These people are all obligated to maintain confidentiality by the nature of their work, or are bound by confidentiality agreements. If required, the study physician may contact your personal physician to collect additional medical information and your past medical history.

The study physician may only share your study information with people whom you have permitted to see it. However once your study information is shared as authorized, it may no longer be protected by Federal law and may be re-disclosed without your permission.

While participating in this study, the study physician will replace your name with a special code that identifies you. This code, along with your study information, will be used by the study sponsor, The Medicines Company and their representatives, for the study purposes mentioned above and to help establish whether the study drug is safe and effective. The Medicines Company may share your coded information, as necessary, with The Medicines Company affiliates who work within the scope of this consent; people and companies who work with The Medicines Company and who work within the scope of this consent; Ethics committees and Regulatory agencies such as the US Food & Drug Administration, the National Health Authorities, and the European Medical Agency.

Study Information, your study code, and samples collected as part of this study will be included in The Medicines Company's secure electronic trial systems. These systems may be managed and monitored by companies who work with The Medicines Company.

You should be aware that some countries may not offer the same level of privacy protection as you are used to in the country where you live or where this study is conducted. However, The Medicines Company will keep any information it receives to the same standard of confidentiality as far as permitted by applicable local law. The Medicines Company has also entered into agreements with third parties working for The Medicines Company to secure adequate protection of your data and samples.

The Study Information will be kept confidential within the limits of the law and used only for research purposes mentioned above. If the results of this study are published or presented in a meeting, you will not be named and nobody will be able to tell that you were in the study from the publication or presentation.

Your participation in this study is voluntary and you may cancel this consent at any time and without any reason. If you do so, your participation in the study will end and the study staff will stop collecting information from you, however, you will be asked to come back to the site for an end of study visit. However, The Medicines Company will continue to retain and use any research results that have already been collected to verify the scientific integrity of the study. If you wish to leave the study inform your study physician.

You have the right to review your Study Information and medical records and request changes to the Study Information if it is not correct. However, please note that during the study, access to Study Information may be limited if it weakens the integrity of the research. You may have access to the Study Information held by the study physician at the end of the study.

If you have any questions about the collection and use of information about you, or would like to exercise rights that you may have regarding this information, you should ask your study physician.

## **GETTING ANSWERS TO YOUR QUESTIONS ABOUT THE STUDY**

You can ask questions about this consent form or the study (before you decide to start the study or at any time during the study). Questions may include, but are not limited to:

- Who to contact in the case of a research-related injury or illness.
- Any payment for being in the study.
- Your rights and your responsibilities as a study subject.
- Other questions.

Contact the study physician or study staff with any questions or concerns. Their telephone number is printed on the first page of this form. If you have any questions or complaints about your rights as a research subject, you may also contact an advisor at an independent research ethics review board that reviews this study:

- By mail:  
Study Subject Adviser  
Chesapeake Research Review, Inc.  
7063 Columbia Gateway Drive, Suite 110  
Columbia, MD 21046

- or call **collect**: 410-884-2900
- or by **email**: [adviser@irbinfo.com](mailto:adviser@irbinfo.com)

Please reference the following number when contacting the Study Subject Adviser: Pro00006192.

### **IS YOUR PARTICIPATION VOLUNTARY?**

Yes, your participation in this study is strictly voluntary. You may refuse to take part in it, or you may stop participating at any time, even after signing this informed consent. There will be no penalty or loss of benefits to which you are otherwise entitled. However, if you decide to leave the study before it ends, the study physician will need to see you before you are released from the study.

The study physician, Sponsor, FDA or Chesapeake Research Review may also decide to remove you from the study at any time without your consent. The study physician may choose to take you out of the study because of unexpected or serious side effects, or for other scientific, technical, or safety considerations.

Examples why you may be taken out of the study are:

- Staying in the study would be harmful
- You need treatment not allowed in this study
- You failed to follow instructions
- You become pregnant
- The study is cancelled
- Your treatment arm is stopped

If your participation ends for any reason, you will return to the study for the following study procedures:

- Physical examination.
- Pregnancy test (if necessary).
- Body weight.
- Blood pressure, respiratory rate, pulse oximetry, pulse rate, and body temperature.
- Safety ECG.
- Blood draws for hematology and chemistry.
- Blood draws for PK.
- Urine will be collected for urinalysis.
- Adverse events and concomitant medications.

If you should decide to leave the study you should tell the study physician or study staff. They will make sure that proper procedures are followed and a final visit is made for your safety.

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.

**STATEMENT OF CONSENT**

I have read this form and its contents were explained to me. I agree to be in this research study for the purposes listed above. All of my questions were answered to my satisfaction. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing this form.

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Signature of Research Subject

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/\_\_\_\_\_/\_\_\_\_\_  
Date

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Printed Name of Research Subject**STATEMENT OF PERSON EXPLAINING CONSENT**

I have carefully explained to the subject the nature and purpose of the above study. There has been an opportunity for the subject to ask questions about this research study. I have been available to answer any questions that the subject has about this study.

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Signature of Person Explaining Consent

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/\_\_\_\_\_/\_\_\_\_\_  
Date

---

Printed Name of Person Explaining Consent

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/\_\_\_\_\_  
Time (24 hour)

### **HIPAA Authorization Agreement**

#### **Permission to Review, Use and Release Information about You**

If you decide to be in this study, the study physician and research team will use and share health data about you to conduct the study. Health data may include:

- Your name.
- Address.
- Phone number.
- Date of birth.
- Medical history.
- Information from your study visits, including all test results.

Health data may come from your study records or from existing records kept by your doctor or other health care workers.

For this study, the research team may share health data about you with authorized users. Authorized users may include:

- Representatives of The Medicines Company.
- Representatives of Spaulding Clinical Research, LLC.
- Representatives of Chesapeake Research Review, Inc. (an independent research ethics review board that reviews this study).
- The Food and Drug Administration (FDA) and other US governmental agencies.
- Government agencies to whom certain diseases (like HIV, hepatitis, and STIs) must be reported.
- Governmental agencies of other countries.
- Labs working with the sponsor on this study.
- Other authorized users.

The sponsor and those working for the sponsor may use the health data sent to them:

- To see if the study drug works and is safe.
- To compare the study drug to other drugs.
- For other research activities related to the study drug.

Once your health data has been shared with authorized users, it may no longer be protected by federal privacy laws.

Your permission to use and share health data about you will not end unless required by state law. If state law applies, your permission to use and share health data about you will end on December 31, 2060.

You may take back your permission to use and share health data about you at any time by writing to the study physician. If you do this, you will not be able to stay in this study. No new health data that identifies you will be gathered after your written request is received. However, health data about you that has already been gathered may still be used and given to others as described in this form.

Your right to access your health data in the study records will be suspended during the study to keep from changing the study results. When the study is over, you can access your study health data.

If you decide not to sign this form, you will not be able to take part in the study.

### STATEMENT OF AUTHORIZATION

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing this form.

\_\_\_\_\_  
Signature of Research Subject

\_\_\_\_/\_\_\_\_/\_\_\_\_  
Date

\_\_\_\_\_  
Printed Name of Research Subject

### STATEMENT OF PERSON EXPLAINING AUTHORIZATION

I have carefully explained to the subject the nature and purpose of this form. I have been available to answer any questions that the subject has about this form.

\_\_\_\_\_  
Signature of Person Explaining Authorization

\_\_\_\_/\_\_\_\_/\_\_\_\_  
Date

\_\_\_\_\_  
Printed Name of Person Explaining Authorization