

Study Drug: Dalbavancin
Protocol No. VER001-19
MDS Pharma Services Project No. AA15712

INFORMED CONSENT

MDS PHARMA SERVICES

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STUDY TITLE: A Phase I Study to Evaluate the Distribution and Excretion of Intravenous Dalbavancin in Healthy Subjects After a Single Dose

Giving false, incomplete, or misleading information about your medical history, including past and present usage of other medications, could have very serious consequences for your well being. It is important that you give a true and complete medical history.

You are being asked to participate in a research study. The people who take part in research studies are called subjects. You should read this form before you decide to take part in the study. This form will tell you about the study. Ask the study staff as many questions as needed for you to decide if you want to take part in the study. We will give you a copy of this form. You may have questions about the study later. If the answer is not in this form, there are names and telephone numbers of people you can call to get answers.

1. PURPOSE OF THE STUDY

The purpose of this study is to find out the amount of dalbavancin in your blood, urine, feces, and skin blister fluid after you receive a single intravenous (IV) dose of dalbavancin.

Dalbavancin is not approved by the FDA (US Food and Drug Administration) for use and is currently being studied as a potential antibiotic for the treatment of bacterial infections.

During this study, Cantharidin ointment will be used to create a blister on your skin. Cantharidin ointment is not approved by the FDA for use but it can be used for the treatment and removal of warts in a doctor's office. It will only be used topically (on the skin) to create a blister that will later be sampled to find out the amount of dalbavancin in the blister fluid.

2. QUALIFYING TO BE IN THE STUDY

The study doctor will review all of your medical information and findings from your screening visit (including medical history, medications, clinical laboratory results, physical exam, etc.) to determine if you are eligible to participate in this study.

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To help the Study Doctor and the Sponsor find out if you qualify for this study and if it is safe for you to take part, you need to be seen at the clinic within 21 days before the study starts. You will have the following screening procedures done:

- **General Information:** We will need to know your name, age, date of birth, sex, race, address, social security number, and phone number.
- **Medical history:** We will ask you questions about your past and current health, surgeries, allergies, prescription and over-the-counter drug use, alcohol use, and tobacco use. We may ask you other questions about your lifestyle or habits that can have an effect on your health such as: diet, caffeine use, exercise, birth control, your job, other research studies you have been in, and blood or plasma donation. We may ask questions about the health of your blood relatives. You can ask the study staff questions about any forms or questions you do not understand.
- **Physical Examination:** Your blood pressure, temperature, heart rate, rate of breathing, height, and weight will be measured. A doctor will examine you and may ask you more questions about your health and lifestyle.
- **Blood and Urine Sample Collection:** Blood will be taken from a vein in your arm using a needle. The blood sample will be used to check your general health, including a test for hepatitis B, hepatitis C, and HIV. If you are a female, your blood will also be used for a pregnancy test. The urine sample will be used to check your general health and to test for drugs of abuse and/or alcohol. Some drugs can be detected in the urine for several weeks.

After screening, and if you are accepted in the study, we will tell you what day you will need to start the study. In addition, you will be given a container to collect a fecal sample and instructed how to collect a fecal sample by the study staff. You will be required to bring back the sample before the start of the study.

3. SUBJECT RESPONSIBILITIES

If you are chosen to be on the study, you are responsible for:

- Following general clinic rules.
- Following study instructions given by the staff.
- Following study restrictions.
- Reporting any changes in your physical or mental condition during the study.
- Reporting any side-effects you may have during the study.
- Giving true and complete answers to questions during the study.

A. GENERAL CLINIC RULES

Scheduled clinic meals/snacks will be served. The menu will include meat and dairy products. No foods or beverages containing alcohol, grapefruit, or caffeine will be served. You can eat only the foods and drink provided by the clinic staff. You can eat and drink only at the times food and drink are provided.

Heavy exercise (running, jogging, weight lifting, contact sports, etc) is not allowed in the clinic.

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Sunbathing is not allowed in the clinic.

You must stay in the clinic area assigned for your study.

B. STUDY RESTRICTIONS

The study has restrictions because some drugs, foods, drinks, or activities can increase or decrease the effect of the study drug. This can be a risk to your health and/or lead to false study results. The restrictions for this study are in the following table. A day is 24 hours.

Restriction	Time (in days) before study	Time (in days) during study
Alcohol	2 days before dose	During confinement
Drugs that can increase or decrease the amount of certain drugs in the blood (the study doctor will determine this)	21 days before entry	During the entire study
All other prescription drugs (with the exception of hormonal contraceptives for females)	14 days before entry	During the entire study

Additionally, you cannot take part in another study or give blood (other than for this study) or plasma while being considered for this study or while taking part in this study.

4. LENGTH OF STUDY

The study will last about 71 days. You will stay in the clinic from the evening before the day you receive the study drug through the morning of Day 8. You will also be required to return to the clinic in the mornings of Days 14, 21, 28, 42, 56, and 70, and stay for a 24-hour period. There will be a total of 14 overnight stays during this study.

5. NUMBER OF SUBJECTS

The study will enroll 9 healthy male or female subjects. More subjects may be enrolled if at least 6 subjects do not complete the study.

6. STUDY PROCEDURES

Procedures will be done during the study at assigned times between the first day you enter the study and the last scheduled day of the study.

A. STUDY DRUG

Dalbavancin is not approved by the FDA for use and is currently being studied as a potential antibiotic for the treatment of bacterial infections. Since Dalbavancin is an experimental medication, the usual dose is not known. Dalbavancin has been given in single doses from 70 mg to 1120 mg and in multiple doses of 48 mg to 1600 mg a day over 7 days.

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You will receive the study drug by intravenous infusion also known as an IV. An IV is a small needle and catheter (tubing) device inserted into a vein in the arm to allow the study drug to be delivered directly into the blood stream. After the catheter is placed into the vein, the needle will be removed, and the catheter securely taped in place. Following administration of the study drug, the catheter will be removed. The catheter may need to be reinserted during the study if it is dislodged or if the site is inflamed.

The dose planned for this study is 1000 mg.

You will receive the study drug over 30 minutes on the morning of the day of dosing.

B. BLOOD COLLECTION

We will use a needle to take blood samples from a vein in your arm during the study. The samples will help us to find out how much study drug is in your blood and to check your general health. The blood samples can also be used for pregnancy tests if you are a female. We will take blood samples from you 15 times during the study. We will take about 8 ounces of blood from you during the study. We may take more samples if needed to check on your safety.

C. SKIN BLISTER FORMATION AND FLUID COLLECTION

During the study, 5 blisters will be induced on your forearms so that the fluid in the blisters can be tested for the study drug. Blisters will be created on the evening of Day – 1, the morning of Day 1, and the evenings of Days 2, 4, and 6. The fluid from the blisters will be collected, using a small gauge needle, 12 to 14 hours after the cantharidin ointment is applied. Photographs will be taken of the blister site. Blisters will then be covered with gauze.

D. URINE AND FECES COLLECTION

You will provide urine samples during the study to check your general health. The urine sample will also be used to see if you have alcohol or drugs of abuse in your system.

For 7 days after taking the study drug, and on Days 14-15, Days 21-22, Days 28-29, Days 42-43, Days 56-57, and Days 70-71, all of your urine and feces needs to be collected to see how much study drug is in your urine and feces. To make sure that all urine and feces is collected, the restroom doors will be locked during the collection period. The clinic staff will provide you with a labeled container and will unlock the restroom door for you each time you need to enter the restroom.

E. VITAL SIGNS

To find out if you are having any effects from the study drug, and to check your general health, your blood pressure, heart rate, breathing rate, and temperature will be measured during the study.

F. EXAM BY DOCTOR

To find out if you are having any effects from the study drug, and to check your general health, a doctor will examine you during the study.

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G. QUESTIONS FOR YOU

We will ask you questions during the study. Some of the questions will be in a written form. Some of the questions are to find out if you are following the study rules and restrictions. Some of the questions are to find out if you are having any effects from the study drug.

7. RISK OF POSSIBLE DISCOMFORTS OR EFFECTS

There may be risks and discomforts that are not yet known. The known risks, discomfort or effects are described below.

A. STUDY DRUG

Dalbavancin has been well tolerated in healthy subjects administered up to 1120 mg dalbavancin as a single IV dose. Possible side effects are similar to those associated with taking marketed antibiotics that are in the same class of drugs as dalbavancin. Possible side effects may include diarrhea, abdominal pain, heartburn, headache, and low grade fever (37.1-37.5°C).

Side effects reported as related to dalbavancin by investigators include allergic reactions, sleeplessness, sleepiness, fatigue, blood in the urine, protein in the urine, menses delayed (women), nasal congestion, worsening asthma, cough, popular rash, skin itching, rash, worsening hypertension, inflammation of the vein in which dalbavancin is infused, redness at the infusion site, hypersensitivity (allergic reaction), infusion site reaction, infusion site itching, increases in certain blood cells (eosinophils, and platelets), gastrointestinal upset, loose stools, nausea, fungal infection, vaginal candidiasis (women), skin fungal infection, urinary tract infection, fungal vaginosis (women), postoperative wound breakdown, audiogram abnormal, elevation of enzymes found in the liver, increased blood sugar, and dizziness.

There is always a chance that an unexpected side effect may happen to people who take this or any other drug. Medical staff are in the clinic to provide medical attention if needed.

B. Cantharidin Ointment (Topical Use Only)

Cantharidin has been used for many years to produce skin blisters as a treatment of warts. Cantharidin causes skin irritation and blistering. Application to the skin may cause tingling, itching or burning within a few hours and the site may be extremely tender for 2 to 6 days. Scarring rarely occurs when used to remove warts. One case of lymph vessel inflammation was reported in a patient treated with cantharidin and salicylic acid plaster.

Cantharidin is poisonous if swallowed. Even small amounts swallowed can cause burning of the mouth, difficulty in swallowing, nausea, blood in the urine, and difficulty in urination.

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C. SKIN BLISTER FORMATION AND FLUID COLLECTION

Cantharidin ointment will be applied on the forearm to produce a blister of the top layer of skin. Cantharidin is to be applied by the staff and used on the skin only.

You may experience some pain when the skin blisters are created and/or collapsed. There is also a small risk of infection, bleeding, and scarring at the site of each blister.

People with darker skin tones can experience longer healing times.

You may experience tingling, itching or burning within a few hours after application of the cantharidin ointment and the site may be extremely tender for 2 to 6 days.

D. BLOOD COLLECTION

Risks associated with drawing blood from your arm include pain, bruising, swelling, lightheadedness, and on rare occasion, infection and nerve damage (some numbness and tingling).

8. POSSIBLE RISKS TO A FETUS, EMBRYO, OR CHILD WHO IS BREASTFEEDING

It is possible that this drug may cause harm to a fetus or embryo. **If you are a female, and able to become pregnant, you should avoid becoming pregnant during the study.** Unless you have had your uterus and/or both ovaries removed, have had both of your tubes removed, cut, and/or tied, or are 2-years postmenopausal, we consider that you are able to become pregnant.

If you are sexually active and able to become pregnant, the study doctor must approve the method of birth control that you have been using and you must agree to continue using that method of birth control through completion of the study. You could become pregnant even while using an approved method of birth control. Not having sex with a male is the only way to be certain that you will not become pregnant. If your method of birth control is oral contraceptives, you will need to add a barrier method of birth control (ie, diaphragm, condom) during the course of the study.

If you become pregnant during the course of this study, you should notify the investigator as soon as possible, since the risks to pregnant women, the embryo, the fetus and nursing children are unknown.

The medicine a mother takes can also pass into a nursing child through the breast milk. This could cause harmful side effects to the child. The safety of dalbavancin during breast-feeding is not known. **Women who are nursing cannot take part in this study.**

9. NEW FINDINGS DURING THE STUDY

You will be told as soon as possible, in writing, of any new or important findings that develop during this study. This can help you decide if you want to continue in the study.

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10. POSSIBLE BENEFITS FROM THE STUDY

You will not receive any direct medical benefit from taking part in this study. The tests provided at screening may help you in learning about your general health or in finding a medical condition of which you were unaware. Information from this study may help the Sponsor and doctors learn things about dalbavancin that will help others.

11. TAKING PART IN THE STUDY OF YOUR OWN FREE WILL

You will take part in the study by your own choice and your own free will. No one can force you to enter the study. If you enter the study, no one can force you to remain on the study. There will be no penalty or loss of benefits that you are entitled to as a subject if you do not take part in the study or if you leave the study before it is over.

You are being asked to take part in this study because you are healthy. You will not be taking the study drug to treat bacterial infections. The only other choice to taking part in the study is to not take part.

12. COST FOR TAKING PART IN THE STUDY

There are no costs to you for participating in the study. All study drug and study procedures are provided to you at no charge.

13. PAYMENT FOR TAKING PART IN THE STUDY

If you are enrolled and complete the study, MDS Pharma Services will pay you up to \$3,610.00, by check, for your part in the study. If for any reason you do not complete the study, you will be paid on a prorated basis, depending on the reason for not completing and the amount of usable data from your part in the study. No deductions for any state or federal withholding (or any other similar taxes) will be made on your behalf. You are responsible for reporting study payments from MDS Pharma Services on your state and federal tax return for the payment of any taxes due for study payments.

Taking part in this study does not make you an employee of the Sponsor, MDS Pharma Services, or the US Food and Drug Administration.

14. TREATMENT FOR STUDY RELATED INJURY

If you become physically injured or ill as a direct result of taking part in this study, MDS Pharma Services will arrange the medical treatment needed to help in your recovery from the injury or illness. There will be no charge to you for this care beyond what is covered by your health insurance. This medical treatment does not include treatment for any illness or injury you might have during the study if it is not the result of the study. If medical treatment is provided, it does not mean that MDS Pharma Services agrees that your injury or illness is a result of the study. No compensation other than free medical treatment of the injury or illness will be provided.

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15. REASONS YOU CAN BE REMOVED FROM THE STUDY

You can be removed from the study if:

- You do not follow the study instructions given by the staff.
- You do not follow the study restrictions.
- You do not continue to meet the requirements for the study.
- The study doctor decides it is best for your health.

You can decide to remove yourself from the study.

The Sponsor can stop the study at any time or ask us to remove you from the study.

16. LEAVING THE STUDY BEFORE IT IS COMPLETED

If you leave the study before the study is complete, you may be at an increased risk of the effects of the study drug.

If you decide to leave the study while you are in the clinic, please tell a staff member. It may not be safe for you to leave before we ask you some questions and do some things to check your health. You may be asked to complete a form about leaving the study. We may want to have a doctor examine you, measure your vital signs, measure your weight, perform an ECG, and/or collect blood and urine samples for general health screening.

If you decide to leave the study when you are not in the clinic, please call the MDS Pharma Services' 24-hour Nurse's Line at (402) 790-4742. We need to let you know if it is safe for you to leave the study. You may be asked to complete a form about leaving the study. You may need to make a visit to the clinic to check your general health. We may want to have a doctor examine you, measure your vital signs, measure your weight, perform an ECG, and/or collect blood and urine samples for general health screening.

You will not receive the full payment for the study if you leave before it is complete.

17. CONFIDENTIALITY

For the purposes of study reporting, you will be identified by initials and numbers only. Your name, address, telephone number, and your emergency contact information will be kept at MDS Pharma Services in case you need to be contacted in the future about this study. Under certain circumstances, some test results will be reported to health authorities where required by law or statute. The results of this study may be published or shared with other pharmaceutical companies without disclosing your identity.

Information collected during the study, including any photographs will be confidential, to the extent allowed by law, and retained by MDS Pharma Services and the study Sponsor. All of this information is subject to review by the appropriate staff and representatives on behalf of the Sponsor, the Institutional Review Board, and regulatory authorities, such as the US Food and Drug Administration, for verification of clinical procedures and/or data. Your permission for the review of confidential information is granted by signing this document.

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18. WHO WILL ANSWER YOUR QUESTIONS

You can ask the study staff any questions about this form or about the study now. You can also ask the staff questions any time during the study.

If you have any further questions about your rights as a research subject, you can contact **Frank E. Landis Jr., J.D.**, of the MDS Pharma Services Institutional Review Board at **1-800-776-1716**.

If you have any further questions about the study, call MDS Pharma Services' 24-hour Nurse's Line at **(402) 790-4742**.

If you have a question about or need to report a side-effect, adverse reaction, or injury while taking part in this study and you are not in the clinic, call the medical staff for the study. You can call the MDS Pharma Services' 24-hour Nurse's Line at **(402) 790-4742**. If you want to contact the doctor in charge of this study, you can call **Dr. James C. Kisicki** at **(402) 476-2811** or, if after 4:30 p.m. or on weekends, at **(402) 610-0111**. Since the doctor may not always be available right away, you should use the 24-hour Nurse's Line.

19. YOUR CONSENT

Your signature below verifies that:

- You have read this written informed consent document and an MDS Pharma Services staff member has explained it to you.
- You have had the chance to ask questions about the study and all your questions have been answered.
- You understand the information in this informed consent document.
- You agree to take part in the study and give your consent for study procedures.
- You are aware that nothing contained in this informed consent waives any of your legal rights as a subject, nor does it release the Investigator, the Sponsor, MDS Pharma Services, or its agents from any liability for negligence.

You certify that you are between 19 and 65 years of age.

Subject Name (Print): _____

Please date your signature when you sign as: Month, Day, Year.

Subject Signature : _____ Date: _____

20. FOR MDS PHARMA SERVICES STAFF

I have discussed this study with the above subject. This person had an opportunity to ask questions. He/She signed in my presence.

Signature : _____ Date: _____
(Staff member explaining study and ICF)

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