

**INFORMED CONSENT
INFORMATION ABOUT DALBAVANCIN**

R10-2059
Cetero Research

DUR001-101
Durata Therapeutics, Inc.

**A PILOT STUDY TO DETERMINE PLASMA CONCENTRATIONS FOLLOWING
ADMINISTRATION OF DALBAVANCIN 1500 MG
BY INTRAVENOUS INFUSION IN HEALTHY VOLUNTEERS**

I have volunteered to participate in this research study which will evaluate how the body processes the study drug dalbavancin when it is administered as a single intravenous (IV) infusion (the medication is given as an injection into a vein in the arm) to healthy subjects under fasting conditions. I understand Durata Therapeutics, Inc.'s dalbavancin has not been approved by the Food and Drug Administration (FDA). Furthermore, I realize the following explanations are provided for my benefit and I must clearly understand the following information before signing my name to each page.

PRACS Institutional Review Board
Approved

 03-16-11

**THE DRUG BEING STUDIED IS A NEW, EXPERIMENTAL DRUG THAT HAS NOT
BEEN APPROVED BY THE UNITED STATES FOOD AND DRUG
ADMINISTRATION (FDA), THEREFORE ALL POTENTIAL EFFECTS OF THE
DRUG ARE NOT KNOWN AT THIS TIME.**

Dalbavancin is Not Categorized for Pregnancy: The risk of taking this product in pregnant women has not been fully determined from either human studies or animal studies.

**I SHOULD AVOID BECOMING PREGNANT OVER THE COURSE OF THE STUDY.
BECOMING PREGNANT WHILE PARTICIPATING IN A STUDY WILL EXPOSE
ME TO A POTENTIAL LOSS OF THE PREGNANCY, OR OTHER UNKNOWN
EFFECTS ON AN UNBORN CHILD SUCH AS, BUT NOT LIMITED TO, BIRTH
DEFECTS AND PREMATURE DELIVERY.**

I. PURPOSE OF THE STUDY

The purpose of this study is to analyze how an IV infusion of the study drug dalbavancin is handled by the body when it is given to healthy subjects. Dalbavancin is an antibiotic that is being studied as a new treatment option for complicated skin and soft tissue infections.

II. PROCEDURES TO BE USED

A. Overview –

I will receive a single dose (1 x 1500 mg intravenous infusion [IV]) of the study drug dalbavancin during the one dosing period of the study.

There will be 8 volunteers (men and women) participating in the study and it will be done only at Cetero Research.

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B. Duration –

This study consists of 1 confined dosing period of at least 34.5 hours. The study also requires a pre-study screening and a post-study evaluation. Therefore, all study-related activities may occur over a 6 week period.

C. Screening Visit

A staff member will explain all of the study procedures to me and will answer any questions or concerns I may have regarding the study. A staff member will ask me medical questions to determine whether I meet the requirements to participate in this study.

I will have a medication and medical history taken (I will inform the physician of any current or past medical problems). I will complete a physical examination which will include height and weight measurements, routine blood and urine tests, an electrocardiogram (a recording of the electrical activity of the heart), blood pressure, heart rate, breathing rate, and temperature evaluations, and screens for **drugs of abuse, tobacco use, alcohol use, pregnancy (females only), FSH (if necessary to document postmenopausal status), hepatitis B, hepatitis C, and AIDS (HIV testing)** before being accepted for this study.

D. Treatment Period –

Day -1

I will report to the research unit by approximately 8:00 PM and will be confined to the research unit until after the 24 hour blood sample collection on Day 2.

At check-in and at any time during my stay at the research unit **my personal belongings may be searched for contraband** (such as food, beverages, chewing gum, candy, medications, strong smelling substances, or any item considered a weapon). Contraband is not allowed inside the research unit. Also, during my stay at the research unit, I will not be allowed to have visitors. All meals during my stay will be provided by the research unit and I will eat only the food provided at the scheduled meal times. **At check-in, a urine sample will be collected for a tobacco and drug abuse screen (all subjects) and a blood sample will be collected for a pregnancy screen (females only).**

Day 1

If dosing is scheduled for 8:00 AM, the following schedule will apply. **This is an example only.** The schedule of events will be dependent on dosing time. For example: After an overnight fast, I will be awakened by 6:45 AM in preparation for medication dosing at 8:00 AM.

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A single dose of study drug will be given through a catheter (a small plastic tube that will be placed into a vein in my arm the evening prior to dosing). The IV catheter will be checked prior to dosing and may be changed if necessary. The study drug will be given over approximately 30 minutes.

Blood samples will be collected within 90 minutes prior to the start of the infusion (0 hour), 20 minutes after the start of the infusion, immediately following the end of the infusion, and at 1, 2, 3, 4, 6, 8, 10, 12, 16, and 24 hours after the start of the infusion.

I will have my blood pressure, heart rate, and breathing rate checked prior to dosing and at 1, 12, and 24 hours after the start of the infusion. I will have my oral temperature taken prior to dosing and at 1, 6, 12, 18, and 24 hours after the start of the infusion. Additional measurements may be obtained.

Day 2

I will be able to leave the research unit after completion of study related activities on Day 2.

Exit Procedures

Following completion of study related activities on Day 2, I will have exit procedures performed after the 24 hour blood sample collection. I must complete all exit procedures which will include blood pressure, heart rate, breathing rate, and temperature evaluations, clinical laboratory tests, and a pregnancy screen (females only). If requested by the investigator(s), I will complete a physical examination.

Any out of range clinical laboratory tests or ongoing adverse events will be followed until resolution, at which time my study participation will be considered complete.

Follow-up Phone Call

Approximately 14 (± 3) days after dose administration, I will be contacted by telephone for follow-up. I will be asked about any medication that I have taken, how I have been feeling, and if I have had any adverse (unusual) events since the last study visit.

E. Over the Course of the Study

During the study, I will be periodically asked how I am feeling.

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Blood samples will be collected by direct blood draw for laboratory screening, pregnancy screen (females only), and drug sample collections:

- For male subjects, blood samples will be collected 15 times
- For female subjects, blood samples will be collected 16 times

The total amount of blood drawn should not exceed 200 mL or about two thirds of a can of soda pop.

F. Requirements for participation –

I understand I must be 18 to 55 years of age, inclusive.

If female, participants must be either:

- naturally postmenopausal (no menses) for at least 1 year and if younger than 55 years of age has a documented FSH level to support postmenopausal status; **or**
- surgically postmenopausal (bilateral oophorectomy [both ovaries removed] or hysterectomy [uterus removed]); **or**

Female subjects that are surgically postmenopausal must provide documentation of the bilateral oophorectomy or hysterectomy prior to dosing or must agree to use a medically acceptable non-hormonal method of birth control.

- surgically sterile (bilateral tubal ligation [tubes tied]) or the Essure[®] procedure; **or**

Female subjects that are surgically sterile must provide documentation of the bilateral tubal ligation prior to dosing or must agree to use a medically acceptable non-hormonal method of birth control. The Essure[®] Procedure must have been inserted at least 3 months with documentation of the Essure[®] confirmation test provided prior to dosing. If the procedure was inserted less than 3 months prior to dosing or proper documentation is not provided, the subject must agree to use an additional non-hormonal medically acceptable method of birth control.

- practicing a medically acceptable method of birth control.

Female subjects of childbearing potential must be practicing and agree to utilize one of the following methods of contraception beginning from screening until 2 months after study completion:

- oral contraceptives (e.g. birth control pills) – must have been used for at least 2 cycles prior to dosing
- condom and spermicide (foam, cream, gel, sponge)

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- condom and diaphragm
- diaphragm and spermicide (foam, cream, gel)
- intrauterine device (IUD)
- complete abstinence

If abstinence is my chosen method of birth control, I agree not to have sex over the course of the study.

I have been informed I cannot enter this study if I have a history or evidence of serious medical problems involving the kidneys, digestive system, heart and blood vessels, lungs, liver, eyes, nerves, brain, skin, thyroid, bones or blood; or such diseases as glaucoma, epilepsy, psychosis, mental illness such as a personal history of depression, diabetes, cancer, tuberculosis, asthma, a blood disease or autoimmune problems. I will also be excluded if I have a history of alcoholism or drug abuse within the past year; use or have used tobacco or nicotine products within the past 6 months; or have a significant history of allergies; or allergies to or adverse experiences with dalbavancin, glycopeptides (e.g. vancomycin), or other related medications.

I have been informed I must comply with the following:

1. **No investigational drug** within **28 days** prior to dosing and throughout the study.
2. **No prescription medications or drugs** should be taken for **14 days** prior to dosing and throughout the study, with the exception of oral hormonal contraceptives (e.g. birth control pills) for female subjects.
3. **No over-the-counter medications or drugs** including aspirin, ibuprofen, or naproxen should be taken for **14 days** prior to dosing and throughout the study, with the exception of acetaminophen (treatment with up to 3 doses \leq 1 gram each dose is permitted from 14 days through 72 hours prior to check-in on Day -1) or spermicide.
4. **No drug or substance known to inhibit CYP enzymes** (quinidine [Quinidex[®]], ketoconazole [Nizoral[®]], fluconazole [Diflucan[®]], cimetidine [Tagamet[®]]) within **14 days** prior to dosing and throughout the study.
5. **No drug or substance known to induce CYP enzymes** (rifampin [Rifadin[®]], phenytoin [Dilantin[®]], carbamazepine [Tegretol[®]], omeprazole [Prilosec[®]]) within **28 days** prior to dosing and throughout the study.

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6. **No herbal or dietary supplements (including St. John's Wort)** should be taken for **14 days** prior to dosing and throughout the study.
7. **No therapeutic dose of any vitamins** should be taken for **14 days** prior to dosing and throughout the study.
8. Standard daily dose multivitamins (non-therapeutic doses) may be consumed until initial check-in and will be restricted until the end of the study.
9. **No medication will be allowed during the study** without first obtaining the approval of the investigator(s).
10. **No caffeine or xanthine such as coffee, tea, chocolate, and all caffeine- or xanthine-containing soft drinks or energy drinks** should be consumed for **48 hours** prior to dosing and during the period when blood samples are collected.
11. **No beverages containing more than 5% juice** should be consumed for **48 hours** prior to dosing and during the period when blood samples are collected.
12. **No grapefruit-, Seville orange-, or pomelo-containing products** should be consumed for **14 days** prior to dosing and throughout the study until the last blood samples are collected.
13. **No alcoholic beverages and/or other alcohol-containing products** should be consumed for **48 hours** prior to dosing and during the period when blood samples are collected.
14. **No food products containing poppy seeds** should be consumed for **48 hours** prior to dosing and during the period when blood samples are collected.
15. **I should not participate if I have donated blood** within **28 days** prior to dosing and I should not donate blood until 4 weeks after completing the study.
16. **I should not participate if I have donated plasma** (via plasmapheresis) within **14 days** prior to dosing and I should not donate plasma until 4 weeks after completing the study.
17. **I should not participate if I have an intolerance of direct venipuncture or if I have veins unsuitable for IV puncture on either arm** (i.e. difficult to locate, access, or puncture, or veins with a tendency to rupture during or after puncture).

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18. **I should not participate if I have difficulty fasting or consuming a standard meal.**
19. **I will not be allowed to participate if I test positive for drugs of abuse, tobacco, or alcohol.**
20. **I will not be allowed to participate if I have a history of fainting, collapse, syncope (loss of consciousness), orthostatic hypotension (low blood pressure upon standing), or vasovagal reactions (brief loss of consciousness caused by a sudden drop in heart rate and blood pressure).**
21. **I will not be allowed to participate if I have a clinically significant illness within 28 days prior to dosing as determined by the investigator(s).**
22. **I will not be allowed to participate if I have any clinically significant results from laboratory tests, vital sign measurements, and electrocardiograms, as determined by the investigator(s).**
23. **I will not be allowed to participate for any reason which, in the opinion of the investigator(s), would prevent me from safely participating in the study.**
24. **I should not participate if I am pregnant, lactating, breastfeeding, or intend to become pregnant over the course of the study (females only).**
25. **My medication history over the past month will be reviewed and I may not participate if any of the medications may change how drugs are absorbed or eliminated.**

III. INCONVENIENCES AND POSSIBLE ADVERSE EVENTS

A. Inconveniences –

I will not be allowed to consume the following products 48 hours prior to dosing and during the period when blood samples are collected:

- caffeine or xanthine products such as coffee, tea, chocolate, soft drinks, or energy drinks
- beverages containing more than 5% fruit juice (fruit drinks, fruit punches, fruit cocktails, etc.)
- alcoholic beverages and/or other alcohol-containing products
- food products containing poppy seeds

I will not be allowed to consume the following products 14 days prior to study dosing and during the period when blood samples are collected:

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- grapefruit-, Seville orange-, or pomelo-containing products

I will be confined to the research unit for at least 34.5 hours during the single dosing period and will not be allowed to have visitors during that time.

Reminder: Times listed in this consent are examples only. I will be informed of actual times through a check-in reminder phone call and by study staff once enrolled in the study.

B. Possible Adverse Events -

1. Local pain, bruising, bleeding, and inflammation or infection might occur at the site of the needle stick where blood is drawn. There is also the possibility of dizziness or fainting while my blood is being drawn. Precautions will be taken to minimize these difficulties.
2. The place(s) on my arm where the venous infusion is given may bruise or feel tender or uncomfortable for 2-3 days after the infusion. If bleeding occurs, I should apply pressure to the place on my arm and notify the study staff immediately. Redness, pain, or swelling at the infusion site may occur. If these symptoms worsen, notify the study staff immediately.
3. Adverse events (side effects) are possible with any drug and I might experience some adverse events during this study. In previous studies, adverse events have been associated with the use of dalbavancin and have included (but may not be limited to) the following:
 - anemia (low red blood count)
 - constipation
 - diarrhea
 - fever
 - headache
 - insomnia (inability to sleep)
 - nausea
 - pruritus (severe itching)
 - rash
 - urinary tract infection
 - vomiting
4. Females: There is a slight risk that a pregnancy test could be falsely negative, thus exposing me to a potential loss of pregnancy as well as other unknown effects on a fetus such as but not limited to birth defects and premature

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delivery. I will be withdrawn from the study participation if I become pregnant or have a positive pregnancy screen.

5. I will be informed if any new risks become known during the course of this study. For my own protection, I agree to report any adverse effect I have to Dr. Sprenger, Dr. Copa, or Dr. Godfrey. If I have an adverse effect, Drs. Sprenger/Copa/Godfrey may, for my protection, stop my participation in the study.

IV. BENEFITS

I will receive no medical benefit from participation in this study other than the routine medical and laboratory examination results of my pre-study screening and exit evaluations, if I so request. However, the knowledge gained by this study may contribute to information which would allow the use of the drug in future patient treatment.

I will receive \$600 for successfully completing the study as previously outlined. If I do not complete the study as described, I will be paid on a prorated basis.

V. ALTERNATIVE TREATMENTS

This research study is not for treatment of a medical condition and therefore the only alternative is to not participate.

VI. COMPENSATION AND TREATMENT FOR INJURY

In the unlikely event I sustain a physical injury because of my participation in this study as a direct result of the administration of the drugs or in the drawing of blood samples or other tests, immediate first aid will be supplied to me. All reasonable medical expenses not covered by my personal medical insurance will be paid by Durata Therapeutics, Inc. or Cetero Research provided the expenses are, in fact, due to injury resulting from the investigational study, I have followed the investigational study requirements and I have immediately notified the investigator(s) of the injury. I also understand no financial compensation other than the treatment listed above is available from Durata Therapeutics, Inc. or Cetero Research. I further understand I do not give up any of my legal rights by signing this form. Should I require further information concerning compensation and treatment for injury, I should contact the investigator(s), Craig R. Sprenger, MD at (701) 239-4750, or Alan K. Copa, PharmD at (701) 239-4750 or (701) 371-6735, or Anthony R. Godfrey, PharmD at (701) 239-4750 or (701) 866-3022.

VII. QUESTIONS ABOUT THE STUDY

I have the right to ask Cetero Research staff or Craig R. Sprenger, MD at (701) 239-4750, or Alan K. Copa, PharmD at (701) 239-4750 or (701) 371-6735, or Anthony R. Godfrey, PharmD at (701) 239-4750 or (701) 866-3022 any questions about my rights as a study participant or any questions concerning the potential or known hazards of this study at

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any time without prejudice. I also have the right to withdraw from the study at any time without prejudice. If I withdraw from the study, I understand that any samples or data collected prior to my withdrawal may be utilized and/or analyzed, unless I provide written withdrawal of my consent. If I should decide to withdraw after receiving study medication, I will be required to stay on site and have all safety data required through the end of the study collected. I should also understand participation or the refusal to participate in the study will in no way influence my medical care by the investigator(s) or other medical personnel. I understand my participation in this study may be terminated at any time when in the judgment of the investigator(s), Drs. Sprenger/Copa/Godfrey, it is in my best interest.

I may also contact William Henderson, PhD, Institutional Review Board member, at (701) 239-4750. The Institutional Review Board is an independent ethics committee that reviews the studies conducted at Cetero Research and protects the rights of the subjects.

VIII. CONFIDENTIALITY

The medical information gathered from this study will be submitted to the appropriate representatives of Durata Therapeutics, Inc. and the Food and Drug Administration of the United States Government under the regulations issued by the federal agency and to other regulatory agencies. Representatives from the U.S. Food and Drug Administration and Durata Therapeutics, Inc. may review my medical records to ensure the accuracy of the information submitted by the investigators.

The collection and submission of the medical information from this study to the appropriate representatives of Durata Therapeutics, Inc. and the U.S. Food and Drug Administration will be accomplished with strict adherence to professional standards of confidentiality. My name and address will be filed under adequate security for use in case future follow-up becomes necessary.

IX. HIPAA AUTHORIZATION TO USE AND DISCLOSE PERSONAL HEALTH INFORMATION

A federal regulation known as the Privacy Rule gives me certain rights concerning the privacy of my health information. The Privacy Rule was issued under a law called the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Researchers covered by this regulation are required to get my authorization (permission) to use and disclose (share with others) any health information that could identify me.

If I sign this informed consent form, I am giving permission for the use and disclosure of my health information for purposes of this research study. I do not have to give this permission. However, if I do not, I will not be able to participate in the study.

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A. Who Will Use and Disclose My Health Information?

The investigator and the Study Team (research staff) at Cetero Research may use my health information to conduct, review, and determine the results of the study. The Study Team may also use my information to prepare reports or publications about the study. However, my name will not appear in any report or publication. The Study Team may disclose my information to others, as discussed below.

B. What Health Information Will be Used and Disclosed?

The Study Team will record my medical history, the treatment I receive, and the results of examinations and tests done during the study on study forms. My name will not appear on the study forms. Instead, I will be assigned a subject identification number. The Study Team will send the completed study forms to the study sponsor. This type of information may also be shared with others, as described below.

My medical records may include other health information about me and may include documents that directly identify me. Representatives from the groups identified below may need to look at my medical records to make sure that the information on the study forms are correct or that the study was conducted properly. Reviews like that will take place at the study center or where the medical records are stored and can take place after the study is over.

C. Who Will Receive My Health Information?

My study information may be shared with the following people or groups:

- The study sponsor or its representatives, including companies it hires to provide study-related services
- Researchers who are conducting this study at other study centers.
- The Institutional Review Board (ethics committee) that approved this study and any other committees responsible for overseeing the research.
- Government health agencies (such as the Food and Drug Administration) in the US or other countries.

Representatives from these groups may receive information from my study forms or may review my medical records (as described above) or both.

D. Will My Information Be Protected by the Privacy Rule After It Is Disclosed to Others?

Cetero Research is required by the Privacy Rule to protect my health information. After my information is shared with others, like the study sponsor, it may no longer be protected by the Privacy Rule. The people who receive this information could use it in ways not discussed in this form and could disclose it to others. The

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sponsor will use and disclose my information only for research or regulatory purposes or to prepare research publications. In addition to using it for this study, the sponsor may reanalyze the study data at a later date or combine my information with information from other studies for research purposes not directly related to this study. The goal of any such research would be to learn more about drugs or diseases or to help design better studies in the future. When using the information in these ways, the sponsor may share it with regulatory authorities, other researchers, its business partners, or companies it hires to provide research-related services. However, my name will never appear in any sponsor forms, reports, databases, or publications, or in any future disclosures by the sponsor.

E. What Happens If I Leave the Study Early?

If I stop participating in the study early for any reason, the Study Team will tell the sponsor why. If the Study Team asks me to come to any more study visits and I agree, the Study Team will send the sponsor information from those visits as well. All information collected about me may continue to be used and disclosed.

F. Will My Authorization Ever Expire?

This Authorization does not have an expiration date. The Study Team may need to correct or provide missing information about me even after my study participation is over. The review of my medical records (described above) may also take place after the study is over.

G. May I Take Back My Authorization?

I have the right to take back (revoke) my Authorization at any time by writing to Craig R. Sprenger, MD, Alan K. Copa, PharmD or Anthony R. Godfrey, PharmD at Cetero Research, 4801 Amber Valley Parkway, Fargo, ND 58104. If I revoke my Authorization, the Study Team will not collect any new health information about me. However, they can continue to use and disclose any already collected information if that is necessary for the reliability of the study. The sponsor can also still keep and use any information that it has already received. If I revoke my Authorization, I can no longer continue to participate in the study.

H. May I Look at My Study Information?

I have a right to see and make copies of my medical records. However, to ensure the reliability of the study, I will need to wait to see my study records until the study is completed.

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My participation in this study is entirely voluntary and refusal to participate carries no penalty. I am free to withdraw from the study at any time, also without penalty or prejudice. I have read and understood the preceding information describing the study. All my questions have been answered to my satisfaction. This form is being signed voluntarily by me indicating my desire to participate in the study. I acknowledge I have received a copy of this consent document.

Participant's Signature

Printed Name

_____/_____/_____
Initials Date

Signature of Person Obtaining
Informed Consent

Printed Name

_____/_____
Date