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TIGECYCLINE Study 3074A1-305-WW

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### INFORMED CONSENT TO PARTICIPATE IN A MEDICAL RESEARCH STUDY

**Title of Protocol:** A MULTICENTER, RANDOMIZED, DOUBLE-BLIND  
COMPARISON OF THE SAFETY AND EFFICACY OF  
TIGECYCLINE WITH THOSE OF VANCOMYCIN WITH  
AZTREONAM TO TREAT COMPLICATED SKIN AND SKIN  
STRUCTURE INFECTIONS IN HOSPITALIZED PATIENTS

**PROTOCOL NO.:** 3074A1-305-WW

**SPONSOR:** Wyeth Research

**INVESTIGATOR:** \_\_\_\_\_

**TELEPHONE NO.:** \_\_\_\_\_

**SUBJECT NAME:** \_\_\_\_\_

**SEX:** \_\_\_\_\_

**DATE OF BIRTH:** \_\_\_\_\_

**ADDRESS:** \_\_\_\_\_

**TELEPHONE NO.:** \_\_\_\_\_

**MEDICAL CHART NO.:** \_\_\_\_\_

**EMERGENCY CONTACT PERSON:** \_\_\_\_\_

**EMERGENCY CONTACT NO.:** \_\_\_\_\_

#### DESCRIPTION/PURPOSE OF THE STUDY

You are invited to participate in a medical research study because your doctor has determined that you may be eligible because you have developed a complicated skin and/or skin structure infection. The standard treatment for your skin infection is the administration of infection-fighting drugs called antibiotics.

Before participating in this research study, you should understand the risks and benefits in order to make an informed decision. This consent form provides detailed information about the research study. Your study doctor will also discuss the study with you. Once you understand the study, you will be asked to sign this consent form if you wish to participate. You will be given a signed and dated copy of the form to keep as a record.

The purpose of this study is to compare the safety and the effectiveness of an experimental antibiotic, tigecycline to a combination of approved antibiotics vancomycin and aztreonam, in treating hospitalized patients with complicated skin and skin structure infections. These antibiotics will be given through a vein.

Approximately 500 subjects will participate in this study at approximately 120 centers in Europe, Australia, Taiwan and Africa. Of the 500 patients who enter the study, half will be randomly assigned (like flipping a coin) to receive tigecycline as 'test article', and half will be randomly assigned to receive vancomycin and aztreonam as 'test article.' Your study

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doctor will not know which test article you are receiving while you are participating in the study, but this information will be available if it should be needed.

Tigecycline has not been marketed in Taiwan or any other country.

**DURATION**

The duration of test article administration will depend on the seriousness of your infection as determined by your study doctor. You will be given the antibiotic for at least 5 days, and no more than 14 days. You will also be required to return to the hospital for a follow-up visit no sooner than 2 weeks after the antibiotic is discontinued.

**PROCEDURES**

Before you can start to receive the test article, you will have the following series of tests and procedures to determine whether or not you are able to participate in the study: medical history, physical examination (including height, weight, heart rate, temperature, blood pressure), Electrocardiogram (ECG) to assess the health of your heart, blood draw (for routine tests and to check to see if the infection has gotten into your blood), a blood or urine pregnancy test will be performed for women of childbearing potential, and a tissue sample (or drained fluid/pus) from the site of the infection. This sample is taken by either scraping the surface or through a needle. A photograph of your skin infection will be taken before and after treatment to document the effectiveness of the treatment. If your study doctor suspects (and needs to rule out) that the infection may involve the bone an imaging x-ray scan (or other suitable imaging scan) may need to be performed. If any type of bone scan is required your study doctor will discuss the procedure and risks associated with the procedure in detail with you.

**TREATMENT**

If you are found to be eligible for the study you will receive infusions through a vein for approximately 2 hours twice a day. If you are assigned to the group that receives the standard antibiotics, vancomycin and aztreonam the dosing consists of 1 g vancomycin followed by 2 g aztreonam every 12 hours. If you are assigned to the group that receives the experimental drug, tigecycline the test article administration consists of a one-time dose of 100 mg of tigecycline followed by 50 mg every 12 hours thereafter (total daily dose of 100 mg). Following the completion of each tigecycline infusion, you will receive a second infusion of 100 mL of a solution (called a placebo, an inactive solution that contains no medication) so that neither you nor your study doctor can tell which test article you receive. If the organism that is causing your skin infection is not sensitive to the test article you receive (based on tests performed on the tissue/pus sample collected) your study doctor may choose to discontinue that treatment and provide suitable alternative treatment.

The period of test article administration will last at least 5 days but not more than 14 days. You will remain hospitalized during this time. Your temperature, heart rate and blood pressure will be taken and your skin infection will be assessed on a daily basis. Blood samples will be taken on Days 3 and 7, and on the last day of treatment. Not more than 100

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mL (5 tablespoons) of blood will be drawn for study purposes throughout the 4 to 6-week study period.

An ECG will be performed between day 3 to day 7. You will be asked to return to your study doctor's office for one additional visit at least two weeks after the infusions have stopped. It is important that this follow-up visit be completed. The blood tests and an ECG will be repeated at the follow-up visit and your skin infection will be reevaluated. A photo of your skin infection may be taken.

**RISKS ASSOCIATED WITH THE STUDY**

All medications have the potential to cause side effects including allergic reactions, which may be severe, and even life threatening. However, precautions will be taken to reduce the risks. You should not participate in this study if you have any of the following conditions:

- history of allergies to tetracycline, or a tetracycline-like drug or vancomycin or aztreonam like drugs
- severe kidney, heart, lung, or liver disease
- history of bleeding disorders

You should discuss all of your past and present diseases and allergies with your study doctor. If you have any questions regarding diseases and/or allergies that you may have had in the past, ask your study doctor.

The most common side effects of tigecycline are nausea, vomiting and diarrhea, constipation, stomach upset, headache, dizziness, itching, rash, mild increases in enzymes of the liver, and swelling of the hands and feet. Pain can occur at the site where the medication is injected into your vein. In addition, the following symptoms have been reported: severe rash, severe diarrhea called colitis, pulmonary edema (excess fluid in the lungs), and decreased kidney functions.

Tigecycline is related to an antibiotic called minocycline and a group of antibiotics called the tetracyclines. The most common side effects that occur with the use of minocycline and tetracyclines are the loss of appetite, nausea, vomiting, diarrhea, yeast infections in the anal and genital areas, and rashes. Other rare reactions have been reported including photosensitivity (a severe sunburn), liver failure, and pseudotumor cerebri (benign intracranial hypertension) with headache and blurred vision as the usual manifestations. This condition and related symptoms usually resolve after discontinuation of the tetracycline, however, the possibility of permanent impairment exists.

Tetracyclines can interact with anticoagulants, commonly called "blood thinners" such as warfarin. Tetracyclines can also interfere with the action of penicillins and oral contraceptives.

The most common side effects of vancomycin are usually related to the infusion and may

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include, but are not limited to: an allergy (shortness of breath; closing of your throat; hives; swelling of your lips, face, or tongue; rash; or fainting); or pain and muscle spasm of the chest and back. Numbness and a rash may appear in the arm used for study drug administration. Patients may also experience little or no urine, decreased hearing or ringing in the ears; or severe watery diarrhea and abdominal cramps. Less frequently nausea, dizziness, chills, blood cell abnormalities or a rash may be seen.

The most common side effects of aztreonam include, but are not limited to, inflammation and discomfort at the infusion site, diarrhea, nausea and/or vomiting, and rash. Less frequently low blood pressure, changes in the electrical activity of the heart (ECG abnormalities), blood cell abnormalities, wheezing, difficulty breathing, chest pain, dizziness, confusion, seizure, general body weakness, fever and headache have been reported.

The risks of drawing blood and giving the medication through a vein may include pain and bruising at the puncture site. Fainting may occur. Infection at the blood drawing site and/or at the site where your needle was inserted could occur. If you have imaging x-rays (or other imaging) you will be exposed to radiation. Your study doctor will discuss this with you.

Treatment with the experimental drug, tigecycline, may involve risks that are not known at the present time. Treatment with the antibiotics vancomycin and aztreonam used in this study may also involve unknown risks. You will be informed of any significant new information that could affect your willingness to continue to participate in the study.

**WOMEN OF CHILDBEARING POTENTIAL ONLY**

The tetracycline class of antibiotics can cause fetal harm when administered to a pregnant woman. The use of drugs in the tetracycline class during tooth development (last half of pregnancy, infancy, and childhood to the age of 8 years) may cause permanent discoloration of the teeth (yellow-gray-brown). Enamel damage has been reported. Birth defects have also been reported. Furthermore, the study medication may involve currently unforeseeable risks to pregnant women, the embryo, the fetus, or to children of nursing women. For this reason, all women of childbearing potential are required to undergo pregnancy testing before entering the study and, if they are sexually active, to refrain from sexual relations or to use a medically acceptable contraceptive throughout the study i.e from the time you sign the informed consent form to the follow-up visit. Tetracyclines can interfere with the action of oral contraceptives. Tigecycline, vancomycin and aztreonam are secreted in breast milk. Women who are nursing an infant will not be permitted to enter the study.

If you miss a period or think you might be pregnant during the study, you must notify the investigator immediately so that you can be withdrawn from the study. If you become pregnant at any time during the study or within 5 weeks after your last dose of the study medication, the study doctor will request your permission to follow the course of your pregnancy and, if carried to term, the delivery as well as the condition of your infant at birth.

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Men who are participating in this research study need to understand the danger of taking a drug whose effects on a fetus are unknown.

#### **BENEFITS ASSOCIATED WITH THE STUDY**

You and other patients with complicated skin infections may benefit from this experimental research. Such benefits include the possibility that your condition may improve and that this study may help develop a new therapy for others with similar conditions.

#### **COSTS AND PAYMENT**

You will not be paid for your participation. You will not incur any additional costs as a participant in this study.

#### **ALTERNATIVE THERAPY**

Other treatments that use different types and combinations of antibiotics are available to treat your condition. Standard treatment at this hospital is [*insert examples of appropriate alternative treatment*]. Their effectiveness varies according to their suitability for an individual patient and the cause of the infection. You do not have to participate in this study to be treated for your skin infection.

#### **CONFIDENTIALITY AND PRIVACY**

The medical staff at this hospital will collect a lot of personal information about you and your medical condition, both generally and in connection with your participation in this trial and use of the test article. In order to verify the results of this research, representatives of Wyeth Taiwan, Wyeth Australia Pty Limited, the US Food and Drug Administration (FDA), other regulatory agencies, and the Independent Ethics Committee (IEC) will be allowed to review your medical records. The information from your medical records will be recorded on forms and sent to Wyeth Taiwan (or its delegates). Your name and address will not appear on these forms; however, your initials and date of birth will be recorded. Your identity will remain confidential unless, for example, disclosure is required by law.

This trial is being conducted to make a scientific assessment of the test article you will receive. In order to do this your de-identified information may be sent overseas for analysis and collation. Information kept at the hospital would allow your identity to be known. However, anybody who does view your identifying information must maintain confidentiality. Nothing containing your identifying information will be intentionally removed from the hospital or clinic.

By signing the attached consent form you specifically consent to the collection of information about yourself as it relates to this clinical trial and to its use. The National Privacy Principles also allow you to have access to personal information collected about you should you wish.

Any report published as a result of this study, which may include photographs, will not reveal your identity.

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**RIGHT TO ASK QUESTIONS AND TO WITHDRAW FROM THE STUDY**

If you have any questions concerning this study, call \_\_\_\_\_ at ( ) \_\_\_\_-\_\_\_\_. If you think you have experienced a research-related injury and if you have any questions concerning the availability of medical care call \_\_\_\_\_ at ( ) \_\_\_\_-\_\_\_\_. If you have any questions about your rights as a research subject, privacy or ethical concerns call \_\_\_\_\_, of the Human Research Ethics Committees at \_\_\_\_\_ (facility) at ( ) \_\_\_\_-\_\_\_\_.

**RESEARCH-RELATED INJURY**

If there is any injury caused by the execution of the protocol, Wyeth Research will be responsible for the indemnity as governed by law.

If you become injured during this study, and your injury is a direct result of the effects of the test article including tigecycline, aztreonam and vancomycin, or any other medication or procedure required for this study *[Insert name of site]* will provide reasonable medical treatment. The cost of this treatment will be paid by the sponsor Wyeth Research, to the extent it is not covered by health insurance. Your participation in this study shall not affect any other rights to compensation you might have under statute or common law.

**VOLUNTARY PARTICIPATION AND CONDITIONS OF WITHDRAWAL**

Your participation in this study is voluntary. You may refuse to participate or you may withdraw at any time without penalty or loss of benefits to which you are otherwise entitled. Your study doctor may withdraw you from the study at any time he or she feels it is in your best interest, without first obtaining your consent.

If you should leave the study for any reason, you may be asked questions about your experience with the test articles. You also may be asked to undergo whatever laboratory tests and physical examinations the study doctor considers necessary for your care.

**CONSENT**

I, \_\_\_\_\_ (*please print name*) have read and understood the preceding information and any questions I have had have been answered to my satisfaction. My signature below indicates that I voluntarily consent to participate in this research study. I do not waive my legal rights by signing this consent form.

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Signature of Patient

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Date of Signature

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Printed Name of Person Administering Consent

\_\_\_\_\_  
Signature of Person Administering Consent

\_\_\_\_\_  
Date of Signature

If applicable: ☐ Yes ☐ No

*(ICH GCP Sec 4.8.8 & 4.8.9)*

\_\_\_\_\_  
Printed Name of Patients legally acceptable representative ☐ and/or Witness to oral consent ☐ and reason applicable

\_\_\_\_\_  
Signature of Representative/Witness

\_\_\_\_\_  
Date of Signature