

Tigecycline 3074A1-306-WW
Prototype version 26 March 2003

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INFORMED CONSENT TO PARTICIPATE IN A MEDICAL RESEARCH STUDY

Title of Protocol: A Multicenter, Double-Blind, Randomized, Comparison Study of the Efficacy and Safety of Tigecycline to Imipenem/Cilastatin to Treat Complicated Intra-Abdominal Infections in Hospitalized Patients (Amendment n°2 short version: incorporating risk section changes)

PROTOCOL NO.: 3074A1-306-WW

SPONSOR: Wyeth Research

INVESTIGATOR: _____

The medical research study for which you have already given your consent has been amended. The amendment will be applied only on the new selected patients but won't apply to you as you have been selected with the previous version of the study.

However the amended informed consent form incorporates modified risk sections. Those sections contain significant new information that may affect your willingness to continue participating in this research study.

The elements of informed consent that have not been included in this amendment are contained in the original consent form for the study in which you are now participating.

RISKS ASSOCIATED WITH THE STUDY

All medications have the potential to cause side effects. There may be risks that we do not know about. However, precautions will be taken to reduce the risks. You should not participate in this study if you have any of the following conditions:

- a history of allergies to tetracycline, or a tetracycline-like drug, or imipenem/cilastatin - like drugs
- severe kidney or liver disease
- history of seizures

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, diarrhea, constipation, stomach upset, headache, dizziness, rash, itching, swelling of the hands and feet. Some patients have had increases in liver enzymes (increases in the values of certain blood tests for liver function). Pain can occur at the site where the study 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.

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Tigecycline is related to an antibiotic called minocycline and a group of antibiotics called the tetracyclines. Following are some of the side effects that have been reported with minocycline and other tetracyclines. It is not known whether all or some of these will be associated with the use of tigecycline, but you should know about them. The most common side effects that occur with the use of minocycline and tetracyclines are dizziness and fever. Other less common or rare side effects include loss of appetite, nausea, vomiting, diarrhea, inflammation (irritation/injury) of the mucous membranes (lining) of the mouth, tooth discoloration, reduced hearing or ringing in the ears, a decrease in white blood cell or platelet counts, eosinophilia (an increase in the number of a specific type of white cell called an eosinophil), redness or pain at the site of injection, increased liver enzymes and hepatitis (inflammation of the liver), a severe allergic reaction, including shock, muscle or joint pain, headache, decrease sensation or tingling, decreased kidney function, cough, shortness of breath, hair loss, increased skin coloring, itching, rashes (rarely including more severe skin reactions, including peeling or blister formation and inflammation of the mucous membranes), skin nodules, hives, sensitivity to light (like a severe sunburn), liver failure, and a condition called pseudotumor cerebri usually resulting in headaches and blurred vision. This condition and related symptoms usually get better after stopping the tetracycline, however, the possibility of permanent injury exists. Syndromes which have been reported with the use of minocycline and tetracyclines include a syndrome similar to a condition called lupus (which can include rash, joint pain, stiffness, swelling, or arthritis, fever, muscle pain, hepatitis and inflammation of blood vessels), a hypersensitivity syndrome (which can include rash, hepatitis, liver failure, fever, lymph node swelling, eosinophilia, and inflammation of the lungs, kidneys, and heart muscle or lining), and a serum sickness like syndrome (which can include fever, rash or hives, eosinophilia, and joint pain, stiffness, swelling, or arthritis). Some of these events have resulted in death.

Patients should use caution when driving a vehicle or using hazardous machinery while receiving a tetracycline because dizziness has been reported.

Tetracyclines can interact with anticoagulants, commonly called "blood thinners" such as warfarin. Tetracyclines can also interfere with the action of penicillins and oral contraceptives ("birth control") by decreasing how well they work. Administration of isotretinoin should be avoided shortly before, during, or shortly after tetracycline administration because it has been associated with pseudotumor cerebri.

The most common side effects of imipenem/cilastatin are stomach and intestinal symptoms such as colitis (severe diarrhea), loss of appetite, nausea, vomiting, diarrhea, rash, itching, fever, dizziness and sleepiness. Allergic reactions, some of which can be severe or life-threatening have occurred. Seizures, increase in the enzymes of the liver, and decreased kidney function can also occur with imipenem/cilastatin. Seizures occur more often when a medication called ganciclovir and imipenem/cilastatin are used together.

Any medication, including the antibiotics used in this research study, can cause an allergic reaction including severe occurrences, in which there can be shock and breathing problems severe enough to be life-threatening.

The antibiotics (tigecycline and imipenem/cilastatin) used in this study may involve other risks that are not known at the present time.

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The risks of drawing blood and giving the antibiotics through a vein include pain and bruising at the puncture site. Fainting may occur. Infection at the site where blood is drawn and/or at the site where your intravenous catheter (small tube) was inserted could occur. If you have x-rays you will be exposed to radiation.

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 study drugs may involve currently unforeseeable risks to pregnant women, the embryo, the fetus, or to children of nursing women. However, tetracycline class 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. 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 and one month after the last study drug intake. Tetracyclines can interfere with the action of oral contraceptives ("birth control") by decreasing how well they work. Tigecycline and imipenem/cilastatin are secreted in breast milk. Women who are nursing an infant will not be permitted to enter the study.

A woman of childbearing potential is defined as one who is biologically capable of becoming pregnant. This includes a woman who is using contraceptives or whose sexual partner is either sterile or using contraceptives.

If you miss a period or think you might be pregnant during the study, you must notify the study doctor immediately so that you can be withdrawn from the study and adequately followed up. If you become pregnant at any time during the study or within one month after your last dose of the study drug (completion or dropout) and your pregnancy is carried to term, the study doctor will follow the course of your pregnancy and delivery as well as the condition of your infant at birth.

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 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.

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If you withdraw from the study for any reason, you may be asked questions about your experience with the study drug you received. You also may be asked to undergo whatever laboratory tests and physical examinations the doctor considers necessary.

CONSENT

I, _____, have read and understood the preceding information. I voluntarily consent to participate in this research study. I do not waive my legal rights by signing this consent form. I will receive a signed and dated copy of this consent form.

Printed Name of Patient

Signature of Patient (Parent/Guardian/Representative)

Date of Signature

Printed Name of Person Administering Consent

Signature of Person Administering Consent

Date of Signature

Patient number : _____
Patient initials : _____
Patient date of birth : _____