

## Patient Information and Consent Form

### LY333328 Study in Skin Infections

#### Introduction

You are invited to take part voluntarily in a research study of an investigational study drug known as LY333328. Your participation in this study is expected to last up to 7 weeks. Up to 900 patients will be participating in this study which will be conducted in a number of hospitals worldwide.

Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and your doctor if you wish. If there is anything you do not understand, please ask. Thank you for reading this.

#### What is the purpose of the study?

The purpose of this study is to determine how LY333328 compares to vancomycin with or without cephalexin (an existing therapy) to see how they improve the symptoms of your skin infection and the side effects they produce.

#### How can I qualify for this study?

Some of the requirements to be in this study are:

- Your doctor has diagnosed you with a type of skin infection allowed by this study.
- You must be at least 18 years of age, weighing at least 37 kg (81 lb).

You cannot participate in this study if —

- You have or have had an illness or condition (as judged by the doctor or as stated by the study) that would not allow your doctor to determine the safety or how well the study medications treat your skin infection.
- You are allergic to certain antibiotics.
- You have recently received antibiotics that may have started to cure your skin infection or you have received experimental treatment within the last 30 days.
- Your veins will not allow dosing with LY333328 or vancomycin (which are given by injection into a vein) or taking of blood.
- You are unwilling to avoid blood and/or blood product (for example, plasma) donation for at least 12 months.

If you are female, in addition to the list above, you cannot be in this study if you are pregnant or breast-feeding.

If you possibly could become pregnant during this study or within the next year, you must talk to your doctor about the method of birth control that you will use to avoid getting pregnant during the study and for 2 months after the last dose of study medication.

Some methods of birth control might be less effective due to a possible interaction with LY333328.

### **Do I have to take part?**

Your taking part in this study is entirely voluntary. You may refuse to take part in the study or you may stop your participation in the study at any time, without a penalty or loss of benefits to which you are otherwise entitled.

Your participation also may be stopped by the study doctor or sponsor without your consent. If this happens, it might be due to a bad reaction you have to LY333328 or new information about LY333328's safety or effectiveness.

If you stop being part of this study, the study doctor or one of the staff members will talk to you about any medical issues regarding the stopping of your participation.

If you agree to take part you will need to visit the doctor's office and/or be assessed at follow-up time periods over 7 weeks.

You do not have to take part in this study to be treated for your illness or condition. Other treatments and therapies for your condition are available. Those might include vancomycin, teicoplanin, quinupristin/dalfopristin, cefazolin, ampicillin with or without gentamicin, or other antibiotics.

### **What will happen to me if I take part?**

If you participate, you will be treated according to the type of skin infection that you have. There are two treatment groups:

- 1) LY333328 given through a small tube inserted in your vein (IV) and sometimes inactive (placebo) given by IV possibly followed by a dummy (placebo) capsule taken by mouth  
  
or
- 2) vancomycin given by IV which may be followed by cephalexin capsules taken by mouth. Cephalexin is another drug used to treat certain infections.

Whether you receive LY333328 or vancomycin will be determined by chance. Two thirds of the patients in this study will receive the investigational medication, LY333328, and the remainder will receive vancomycin.

You will receive IV treatment for a minimum of 3 days and for no longer than 14 days. Depending on the type of your skin infection your doctor will decide if and when to give you the oral study drug for an additional 1 to 7 days. Neither you nor your doctor will know which of the treatments you are receiving. If you agree to participate in this study you will need to stay in the hospital or return to the hospital or an outpatient clinic while you are receiving the IV study medication. Your doctor

will decide how long. Study medication, IV and oral, will not be given for a period longer than 14 days.

Your doctor will perform a physical examination that will include checking your weight, blood pressure, pulse, temperature, and skin infection. A photograph of the infected area may be taken, however no photographs of the face will be taken. A sample from your infected skin area will be taken to identify the bacteria causing your infection. Sometimes a needle or small cut is needed to get the sample. Your examination will also include blood and urine tests, including a test to make sure that you are not pregnant, if you are a woman who can get pregnant. After all this is done, you will be treated with study medication (LY333328 or vancomycin) twice a day.

There are 5 study visits in total, however at any time you get worse or have a new medical problem you should return to your doctor. After the first day of treatment you will be seen for study visits twice in the first week. Two more study visits are scheduled then for 2 weeks and 5 weeks later to check whether your skin infection has cleared. If you are a woman who is able to get pregnant, another test will be done to check you are not pregnant at the end of the study. The last visit may be done by telephone.

Your blood pressure, pulse, and temperature will be checked at each study visit and blood will also be drawn. The total amount of blood taken will be no more than half a pint (approximately one large glass). During the study, your skin infection may be photographed, and fluid or material may be collected from the infected area. You will be examined and asked about side effects and any other medications that you may be taking. If you are given oral medication the container that it came in and any remaining capsules must be returned.

Certain medicines may not be taken while you are on this study. You should talk with your doctor before taking any new medications.

### **What are the side effects of taking part?**

You understand there may be risks for your being in this study. All drugs have side effects. As of 11 September 2000, approximately 356 subjects have taken LY333328. Completed studies and serious adverse events possibly related to study drug in the opinion of the health care provider from ongoing studies are included below.

Possible side effects identified in animal studies include allergic-type reactions (such as rash, redness, flushing, shortness of breath, and low blood pressure), sluggishness, nausea, vomiting, diarrhea, lowered ability to fight infection, and abnormalities in red blood cell count, white blood cell count, liver tests, kidney tests, and some blood clotting tests. In animal studies, these side effects completely or partially reversed following discontinuation of the drug. Rabbits that received LY333328 at 40 mg/kg in a bolus injection (rapid injection of approximately one minute) had possible convulsions, so it will not be given by rapid injection in humans.

Preliminary examination of test-tube data suggests but does not confirm the possibility that LY333328 could cause changes (irregularities) in heart rhythm (arrhythmia). There has been no evidence of life-threatening arrhythmias in animals or in subjects exposed to LY333328 to date.

Of 35 people given single doses of LY333328, adverse events possibly or probably related to LY333328 included headache, strange taste, dizziness, back pain, sleepiness, and rash. Several people had temporary changes in liver tests. LY333328 may interfere with some blood clotting tests, but no bleeding problems have been noted. In two previous studies 27 of 39 people were given multiple doses of LY333328. Thirteen of these people had mild to moderate irritation at the site of injection. One woman out of 10 had vaginitis. Some people also experienced mild abnormalities in liver tests but no symptoms.

In a study of 27 LY333328-treated patients with blood-stream infection, adverse events possibly related to LY333328 included: irritation at the site of infusion (2 patients); decreased red blood cell count (2 patients); flushing (1 patient); faster breathing (1 patient) causing discontinuation of the study drug; kidney function abnormal (1 patient); abdominal pain (1 patient); edema (1 patient); and thrush (1 patient).

In an ongoing blinded (investigator and patient do not know which study medication the patient is receiving) study of 307 patients where patients were given multiple doses of either LY333328 or other antibiotics (vancomycin/cephalexin) for skin infections, one patient experienced acute hepatitis that went away within a month. Another patient in this study had extra heartbeats while receiving study drug; 1 patient with prestudy fluid in the abdominal space and stoppage of the bowels had worsening of these conditions during the study; and 3 patients had serious allergic-type reactions (1 patient with itching and hives, 1 patient with rash, itching, and hives, and 1 patient with itching, rapid pulse, and cold sweats).

Because LY333328 is similar to the antibiotics vancomycin and teicoplanin, people who are known to be allergic to either of these two antibiotics should not receive LY333328. Antibiotics can cause diarrhea with or without blood in some people, so this could also occur with LY333328. LY333328 may stay in the body for a longer period of time than most drugs. Therefore, side effects may take longer to go away.

### ***Risks From Other Study Drugs***

The common bad experiences reported for the other medications (vancomycin or cephalexin) that you might receive during the study are redness or pain where the medicine enters your body, a temporary decrease in cells that fight infection, and temporary lowering of kidney function, diarrhoea, sour stomach, bloated stomach, and abdominal pain. Changes in liver tests have been reported. Less common experiences are a red rash of the upper body, hearing loss, and stomach pain with bloody stools. Rare, but serious experiences that have been reported are severe allergic reaction with decreased blood pressure, difficulty in breathing, severe skin rashes, and kidney failure.

### ***Other Possible Risks***

In addition to the bad experiences named above, LY333328, vancomycin, cephalixin, or the study procedures may have other unknown risks.

There may also be unknown risks to your embryo, fetus, or unborn child. Studies that might show if LY333328 has risks for your embryo, fetus or unborn child have not yet been completed.

For most people, drawing blood samples does not cause any serious problems. However, they may cause bleeding, bruising, discomfort, infections and/or pain at the needle site, or dizziness.

If you have any injury, bad effect, or any other unusual health experience during this study, make sure that you immediately tell the nurses or your doctor. You can call at any time, day or night, to tell us about your health experiences.

There may be unknown risks of possible harmful interaction with other medication you may be taking.

If any important new information is found during this study that may affect your wanting to continue to be part of this study, you will be told about it right away.

### **What if something goes wrong?**

If you follow the directions of the doctors in charge of this study and you are physically injured due to any substance or procedure properly given under the plan for this study, Eli Lilly and Company will pay the medical expenses for the treatment of that injury which are not covered by your medical insurance, by a government program, or by any other third party.

### **What are the possible benefits of taking part?**

You may receive information about your health from any physical examinations and laboratory tests to be done in this study.

Although LY333328 is being tested as a treatment for a condition that you may have, there is no guarantee that you will receive any medical benefit.

You will be paid travel expenses as necessary for follow-up study examinations by your doctor.

Information obtained from this study will benefit the sponsor of the study, Eli Lilly and Company, and may benefit patients in the future.

### **Contact for further information**

If you have any problems, concerns or questions about this study or your rights, please contact: Dr. \_\_\_\_\_ at \_\_\_\_\_ (address), \_\_\_\_\_ (phone #).

If you have any questions about your rights as a participant in a research study, please contact [ERB contact or other neutral or disinterested party] at [address and phone #].

### **Who has reviewed the study?**

In accordance with the Law concerning the safeguard of persons taking part in biomedical research, the \_\_\_\_\_ [*insert Local Research Ethics Committee/ethical review board*] has approved this study.

### **Will my taking part in the study be kept confidential?**

Your medical information will be kept confidential by the study doctor and staff and will not be made publicly available unless disclosure is required by law.

Data obtained from this study that does not identify you individually will be given to the sponsor and/or its representatives and may be published or given to regulatory authorities in [name of country study being conducted in] or other countries in which regulatory approval of LY333328 may be sought.

Your original medical records may be reviewed by Eli Lilly and Company and/or its representatives, the Ethical Review Board for this study, and regulatory authorities for the purpose of verifying clinical trial procedures and/or data. Your medical information may be held and processed on a computer.

By signing this consent form, you authorize the record review, information storage and data transfer described above.

All the data collected during the study will be handled confidentially. They will be coded to protect your anonymity. If the results of the study are published your identity remains confidential and will not be revealed. Your medical information may be held and processed on a computer.

### **Payment to researcher**

The sponsor of this study, Eli Lilly and Company, will pay [insert doctor/ hospital department/research fund] for including you in this study

Thank you for your help.

### **Signatures**

To be entered into the study, you or a legal representative must sign and date the signature page (Attachment 1).

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## Patient Information and Consent Form

### Attachment 1 Signature Page

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#### LY333328 Study in Skin Infections

To become a part of this study, you or your legal representative must sign this page.

By ticking the following boxes and signing this page, you are confirming:

- ☐ You have read and understood all of the information in this Patient Information and Consent Form, and you have had time to think about it.
- ☐ All of your questions have been answered to your satisfaction. If you did not understand any of the words, you asked the study doctor or a staff member to explain them to you.
- ☐ You voluntarily agree to be part of this research study, to follow the study procedures, and to provide necessary information to the doctor, nurses, or other staff members, as requested.
- ☐ You understand that you may freely choose to stop being a part of this study at any time.
- ☐ You have received a copy of this Patient Information and Consent Form to keep for yourself.
- ☐ You agree that your medical records may be directly accessed by Eli Lilly and Company, their designees and by the Regulatory Authorities provided they agree to keep the information confidential.

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Patient Name (Print)

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Patient Initials and Number

**Please write in the date at the time you sign your name.**

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Signature of Patient or Legal Representative

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Date and Time (*patient or legal representation must personally date*)

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Signature of Individual Obtaining Consent

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Date (*individual conducting informed consent discussion must personally date*)