

**Fialuridine (LY303256): Bioequivalence of Syrup and Tablet Formulations, and  
Influence of Timing of Meals on Pharmacokinetic Variables**

**Informed Consent Document**

**INTRODUCTION**

You are invited to take part in a research study of an investigational drug for the treatment of hepatitis B (viral liver infection) known as fialuridine (FIAU, LY303256). We plan to study up to 22 volunteers. Your participation in this study is expected to last up to 4 weeks.

**PURPOSE**

The purposes of this study are to determine how your body handles a syrup form and two tablet forms of FIAU, and to determine the influence of food on how your body handles FIAU.

**PROCEDURES**

Before entering the study you were interviewed by a physician who asked about your medical history and completed a general physical examination. In addition, you have had blood and urine tests done, a heart tracing performed, and may have had a chest x-ray performed if you had not had one within the last six months. Based upon these tests you are being invited to participate in this study.

Your participation in this study will require that you be admitted to the Lilly Clinic. You will receive five single doses of FIAU on five separate dosing days, with each dose being given at approximately 8 AM. Each dose of FIAU will be separated by 3 to 7 days without dosing. Each dose will be 5 mg of FIAU, either as a single 5 mg tablet, as five 1 mg tablets, or as 1 teaspoonful of syrup. On three of the dosing days you will receive one of these dose forms following an overnight fast and will continue to fast for 4 hours after receiving the dose. The total fasting time is up to fifteen hours. On one dosing day you will receive the 5 mg tablet following an overnight fast and immediately before a

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standard breakfast, and on one dosing day you will receive the 5 mg tablet following an overnight fast and at some time between 1 hour before and 2 hours after a standard breakfast.

You will not smoke, or drink caffeine-containing beverages during the study. You will not take any medications (except for an occasional pain medicine) during the study period.

Prior to the start of dosing a blood sample will be obtained. On each dosing day approximately 12 blood specimens will be drawn. A blood specimen for safety analysis will be obtained the day after each dose of FIAU. The total volume of blood collected from you during the study will be about 517 ml, which is about one pint.

### **RISKS**

You understand that there may be risks for your being in this study.

FIAU is a new investigational drug taken for 14 to 28 days by 54 patients with chronic hepatitis B. An additional 100 patients have been treated for up to 8 weeks with a similar drug, FIAC, that is turned into FIAU in humans. Both drugs appear to have similar side effects. These side effects include stomach pain, diarrhea, nausea, vomiting, headache, and muscle aches or fatigue. Changes in laboratory test values that measure liver, kidney, and muscle function, and anemia (low blood count) have also occurred. These laboratory changes are expected to improve, once the study drug is stopped. In addition, laboratory test animals given extremely high doses of FIAU by mouth (3,500 times more than the dose planned for this study, adjusted for different animal weights) have shown decreased sperm production, and animals given extremely high doses directly into their veins (7,000 to 14,000 times more than the dose planned for this study, adjusted for different animal weights) have shown heart muscle damage.

Needle punctures for blood draws are usually well-tolerated by most people. However, they may cause bleeding, bruising, discomfort, infections and/or pain at the needle site and dizziness.

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In addition to these effects, fialuridine (FIAU, LY303256), or the procedures in this study, may have other unknown effects. In case you have any bad effects, make sure that you immediately tell the nurses or Dr. Hyslop at the Lilly Clinic at 276-4757.

You should not participate in this study if you have:

- Concurrent viral infection(s) (AIDS/HIV, hepatitis C, hepatitis D).
- Low blood count tests.
- Received medical therapy for viral infections such as AIDS or hepatitis, including therapy with drugs under investigation as treatment for these infections, within the last six months. Such treatment could include drugs such as zidovudine, didanosine, zalcitabine, and interferon.
- Advanced cirrhosis on liver biopsy or significant liver disease.
- Abused alcohol or drugs within the preceding 6 months.

**VOLUNTARY PARTICIPATION**

Your taking part in this study is entirely voluntary. You may refuse to take part in the study or you may quit the study at any time without a penalty or loss of benefits to which you were entitled before taking part in the study. If you decide to stop being part of this study, Dr. Hyslop will talk to you about the process for stopping and the medical consequences of your making this choice. Dr. Hyslop or Eli Lilly and Company (the sponsor of this study) may stop this study, or your being a part of it at any time without your consent.

**TREATMENT AND COMPENSATION FOR INJURY**

If you follow the directions of the doctor in charge of this study and you are physically injured due to any substance or procedure given during your participation in this study, Eli Lilly and Company will decide either to provide treatment for the injury, or to pay for

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those medical costs that are not covered by your medical insurance. Eli Lilly and Company does not agree to pay any additional money for injury. For further information about compensation or treatment available if injury occurs, contact Dr. Hyslop at 276-4757.

**BENEFITS**

You will be paid for taking part in this study. Since you do not have any of the conditions for which this drug is being developed, you will not medically benefit from being a part of this study. However, information obtained from the study will be of benefit to Eli Lilly and Company and may benefit patients in the future.

**QUESTIONS**

If you have any questions about this study or your rights, please contact Dr. Hyslop at 276-4757. 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.

**CONFIDENTIALITY**

If you agree to participate in this study, the information obtained will be shared with Eli Lilly and Company, the United States Food and Drug Administration, and similar agencies in other countries, all of whom may look at your medical records. Medical records that contain your identity will be treated as confidential by Eli Lilly and Company and will be shared only with these agencies or as required by law.

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This informed consent has been read to me and all my questions have been answered to my satisfaction. I voluntarily agree to be part of this research study. I am between the ages of 21 and 55 years of age inclusive and as far as I know, am healthy.

I understand that I may freely stop being a part of this study at any time.

I have received a copy of this informed consent form to keep for myself. I understand that a copy of this form will also be retained by Eli Lilly and Company.

Volunteer's Name: \_\_\_\_\_

Volunteer's Signature: \_\_\_\_\_

Witness (Investigator): \_\_\_\_\_

Witness (Other): \_\_\_\_\_

Date: \_\_\_\_\_

Time: \_\_\_\_\_

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You will be paid \$25.00 for each day you participate in this study. In addition, if you satisfactorily complete your part in this study, you will receive an additional payment (Satisfactory Completion Payment) calculated at the rate of \$15.00 for each day of your participation.

**Estimated Payment Schedule (calculated for 27 days total participation)**

Hospital stay - 27 days x \$25.00/day =	\$ 675.00
Satisfactory Completion Payment =	\$ 405.00
<b>TOTAL PAYMENT =</b>	<b>\$1080.00</b>

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