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Mar 23, 1995

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Olympia, WA

## PATIENT INFORMATION AND CONSENT FORM

LLH

**STUDY TITLE:** A PROSPECTIVE, RANDOMIZED, MULTI-CENTER, DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL-GROUP COMPARISON OF THE EFFICACY AND SAFETY OF THREE FIXED-DOSES OF SDZ ENA 713, 3 MG, 6 MG, AND 9 MG PER DAY IN PATIENTS WITH PROBABLE MILD TO MODERATE ALZHEIMER'S DISEASE (Pr. B351)

**SPONSOR:** Sandoz Pharmaceuticals Corporation  
East Hanover, New Jersey 07936

**INVESTIGATORS:** Richard L. Borison, M.D., Ph.D.  
Bruce I. Diamond, Ph.D.  
(706) 722-2077

**SITES:** BioTech Park  
1021 15th Street  
Suite 7  
Augusta, Georgia 30901

Medical College of Georgia  
1515 Pope Avenue  
Augusta, GA 30912-3800

**NAME OF PATIENT:** Lewis Huckeba

This consent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand.

This patient information and consent form is for use in a research study which may involve both patients who do and do not have the legal capacity to consent to their participation. Accordingly, when the patient cannot legally consent to participate, the pronouns "you" and "your" should be read as referring to the patient rather than the legally authorized representative who is signing the form to give consent for the patient.

INTRODUCTION

SDZ ENA 713 is a medication being tested for the treatment of Alzheimer's disease.

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You have been asked to participate in this study because you have been diagnosed with Alzheimer's disease. You will be one of approximately 60 patients at this clinic to participate, and approximately 600 people with Alzheimer's disease will participate in this study nationwide. The sponsor of this research study is Sandoz Pharmaceuticals Corporation, East Hanover, New Jersey 07936.

#### PURPOSE OF STUDY

The purpose of this research study is to compare the safety, effectiveness and tolerability of three dose levels of SDZ ENA 713 (3 mg, 6 mg, and 9 mg) to an inactive test substance (placebo) when given to outpatients with Alzheimer's disease. SDZ ENA 713 has not been approved by the U.S. Food and Drug Administration (FDA).

#### DESCRIPTION OF THE STUDY

The study will take approximately six (6) months to complete. You will discontinue any medication(s) that you are currently taking for your Alzheimer's disease. In order to measure the effectiveness of SDZ ENA 713 some patients will receive an inactive drug (placebo) throughout the study. Neither you nor the study doctor will know which treatment you are receiving; however, that information is available if needed.

A number of tests and procedures will be performed to determine if you are eligible for the study. These tests and procedures will include: a medical and neurological history, a physical exam, neurological exam, and an electrocardiogram (ECG). In addition, one tablespoon of blood will be drawn and a urine specimen will be collected for routine clinical laboratory tests. Your urine will be tested to determine the presence of certain drugs. These drugs include amphetamines, barbiturates, benzodiazepines, cocaine, cannabinoids (marijuana), narcotics, and phencyclidine. You must also have had a scan of your head performed within the last one year. If these have not been done, these tests will be scheduled for you. At this first visit, you will also undergo neuropsychological testing, which consists of paper and pencil types of tests that look at how your memory is functioning.

If the tests mentioned above show that you are qualified for the study, you will begin taking study medication. You will be assigned randomly (similar to the flip of a coin) to either one of three dose levels of SDZ ENA 713 (3 mg, 6 mg, or 9 mg/day) or placebo during the next six months. During the first three months your dose of medicine will be slowly increased according to how well you tolerate the medicine. During the second three months your dose of medicine will be held constant. If you are assigned

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to receive placebo medication, you will continue to receive placebo medication during this same period of the study.

During the first three months of the study you will be seen every week. Heart rate, blood pressure, and temperature measurements will be obtained at each study visit. At each visit you will be checked for side-effects. During the second three month period, you will receive neuropsychological testing approximately once each month to see if you are improving. Blood samples of one tablespoon each will be drawn approximately every two weeks for laboratory testing. Electrocardiograms (ECGs) will also be obtained periodically, every 2 to 4 weeks throughout the study, on approximately 8 occasions.

Discharge procedures will be conducted at the end of the study or earlier if you are discontinued before the end of the study for any reason. These discharge procedures will include: a physical exam, neurological exam, heart rate, blood pressure, and temperature measurements, neuropsychological testing, and an ECG will be performed, and a blood sample will be obtained for laboratory testing.

SDZ ENA 713 or placebo is taken twice a day, and should be taken with meals. It is important that you take all the capsules that the study personnel give to you, and return your unused medicine at every study visit. The medication will be provided to you in non-safety closure blister packs.

You will be asked to come in for the follow-up visits at week 12, 18 and 26, even if you discontinued from the study. These visits will be for effectiveness evaluation and after completion of these visits, you could be able to participate in the 26 week open label extension.

If, after completing 26 weeks of double-blind treatment, you wish to continue receiving treatment, you will be offered 26 weeks of open-label ENA 713, during which time you will be receiving ENA 713 and not placebo.

#### POTENTIAL RISKS

Other unexpected and unforeseen side effects may occur. In the people who have already received SDZ ENA 713, the most common side effects that have been reported include: nausea, vomiting, diarrhea, dizziness, sweating, stomach pain, headache, weakness, tiredness, upset stomach, sleeplessness, aggression, agitation, gas, low blood pressure, high blood pressure, and general physical discomfort. Some, all, or none of these side effects may occur

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while you are taking SDZ ENA 713. Some of these side effects occurred at doses of study medicine higher than what you will be receiving, and some of these side effects occurred in patients taking placebo. If you develop these or other side effects, you must notify your study doctor immediately.

You will be told of any developments during the study that may influence your willingness to continue participation.

Since the side effects to the newborn are unknown, if you are a female, you may only participate in this study if you are not of childbearing capacity, due to radiation, surgery, or being postmenopausal for at least two years.

If, in the opinion of your study doctor, there are problems caused by the study medication that make it unwise for you to continue taking it, the medication will be stopped and you will be treated with alternative therapies the same or similar to what you were receiving previously for the treatment of your condition. You may also decide to stop the medication at any time.

Your condition may not improve or may worsen while participating in the study.

#### POTENTIAL BENEFITS

No benefits can be guaranteed to you for your participation in this study. However, if SDZ ENA 713 proves to be effective, it may treat some of the symptoms of your Alzheimer's disease. You will not be charged for any of the medicines, doctor's visits or procedures associated with this study.

#### ALTERNATIVES

The medication tacrine hydrochloride (Cognex®) has recently become commercially available and may help some individuals with Alzheimer's disease. If you choose not to enroll in this study, you may continue taking your current medication or take another medication or combination of medications that are presently sold in the United States. Social services programs may also be available in your area. You do not have to participate in this study to receive treatment for Alzheimer's.

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COMPENSATION FOR INJURY

Except as stated below, Sandoz Pharmaceuticals Corporation will reimburse you for reasonable and necessary medical expenses incurred by you for immediate medical care, including hospitalization, in the treatment of adverse reactions arising directly from the study drugs or devices following their administration or use in accordance with the protocol (study plan). Sandoz Pharmaceuticals Corporation will not reimburse you for the medical expenses identified above if such expenses are covered by your medical or hospital insurance coverage or other third party payor, or if your injuries or adverse reactions are the result of the negligence or misconduct of any person not employed by the sponsor or if your injuries or adverse reactions are the result of your failure to follow the instructions of the study doctor or his staff. The study doctor and his staff are not employees of Sandoz Pharmaceuticals Corporation.

VOLUNTARY PARTICIPATION/WITHDRAWAL

Your participation in this research study is voluntary. You may refuse to participate or you are free to withdraw from the study at any time without affecting your medical care. Refusal to participate in this study will in no way jeopardize your medical care.

Your participation in this study may also be discontinued, without your consent, by your study doctor or by the sponsoring company (Sandoz Pharmaceuticals Corporation) for failure to follow your study doctor's instructions; or if, in the study doctor's opinion, you are not doing well or your safety or well-being is in question. If you decide to stop the study on your own, you must immediately notify your study doctor. If you discontinue the study early because of side effects, you will be asked to return for interviews and memory tests at weeks 12, 18, and 26. If you comply with this request and wish to receive treatment, you will be offered 26 weeks of open-label ENA 713.

QUESTIONS

If you have any questions about the research, you may contact Richard L. Borison, M.D., Ph.D. or Bruce I. Diamond, Ph.D. at (706) 722-2077.

If you suffer a research-related injury or if you have medical questions, contact Richard L. Borison, M.D., Ph.D. at (706) 722-2077.

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If you have any questions about your rights as a research patient, contact the Western Institutional Review Board® (WIRB®), 3535 7th Avenue, S.W., P.O. Box 10160, Olympia, Washington 98502, Telephone: 1-800-562-4789.

Do not sign this form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

**CONFIDENTIALITY**

Information from this study will be submitted to the sponsor and to the U.S. Food and Drug Administration (FDA). It may be submitted to governmental agencies in other countries where the study drug may be considered for approval. Medical records which identify you and the consent form signed by you, will be inspected by the sponsor, International Clinical Research Corp. (ICRC) (an agent for the sponsor) and may be inspected by the FDA and the Western Institutional Review Board® (WIRB®). Because of the need to release information to these parties, absolute confidentiality cannot be guaranteed. The results of this research project may be presented at meetings or in publications; however, your identity will not be disclosed in those presentations.

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CONSENT

I, Lewis Huckeba, HAVE READ THE INFORMATION ABOVE AND HAVE HAD THE STUDY FULLY EXPLAINED TO ME. ANY QUESTIONS THAT HAVE OCCURRED TO ME HAVE BEEN FULLY ANSWERED BY THE STUDY DOCTOR IN CHARGE OF THE STUDY. I VOLUNTARILY GIVE MY CONSENT TO TAKE PART IN THE STUDY OF SDZ ENA 713 IN THE TREATMENT OF ALZHEIMER'S DISEASE.

I UNDERSTAND THAT I WILL RECEIVE A COPY OF THIS CONSENT FORM.

I AUTHORIZE THE RELEASE OF MY MEDICAL RECORDS TO THE SPONSOR, ICRC, THE FDA AND WIRB\*.

BY SIGNING THIS FORM I HAVE NOT WAIVED ANY OF THE LEGAL RIGHTS WHICH I OTHERWISE WOULD HAVE AS A PARTICIPANT IN A RESEARCH STUDY.

Lewis L. Huckeba  
Patient's Signature

4/21/95  
Date

Lewis L. Huckeba  
Patient's Name (Please Print)

\_\_\_\_\_  
Legally Authorized Representative  
(If Applicable)

\_\_\_\_\_  
Date

Debra S. Brown  
Witnessed By

4/21/95  
Date

Debra S. Brown  
Witness' Name (Please Print)

[Signature]  
Signature of Investigator

4-21-95  
Date

wirb/sandoz/ejaw  
corr. 11/22/94/ejaw  
mod. 1/27/95/klh  
mod. 3/23/95/akm

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CAREGIVER INFORMATION

As the patient's caregiver, you have the important responsibilities indicated below.

1. You must accompany the patient to all clinic visits.
2. You will receive a schedule for clinic appointments from the study doctor or his assistant. You must try to keep all scheduled appointments because the day and time of the appointment are important to the study doctor's evaluation of the patient.
3. You will be responsible for the storage and administration of the study drug. You must ensure that the patient takes each dose of medication. You must store the drug safely. You must return all supplies, including medication and the packaging from used medication, to the study doctor when you bring the patient in for a clinic visit.
4. You are a very valuable source of information about the patient. The study doctor will interview you during each clinic visit in order to find out if the study medication is producing any changes in the patient. Your cooperation in answering these questions is necessary.

If for some reason you become unable to fulfill your responsibilities, please notify the study doctor immediately. If possible, you may be asked to designate a substitute who can take over your duties for the period necessary.

CAREGIVER'S CONSENT

I, Janis M. Huckeba (print caregiver's name) have read and I understand all of the preceding information which describes both the patient's participation in the study and my responsibilities as the patient's caregiver. I voluntarily consent to participate in the study.

Janis M. Huckeba  
Signature of Caregiver

4-21-95  
Date

Delia A. Brown  
Signature of Witness

4/21/98  
Date

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