Suppressive Antibacterial Therapy with Once-weekly Solosec®(secnidazole) Oral Granules to Prevent Recurrent Bacterial Vaginosis

Drug Name: Solosec®(secnidazole) Oral Granules, 2 g

NCT # 05033743

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INDIANA UNIVERSITY INFORMED CONSENT STATEMENT FOR RESEARCH

Suppressive Antibacterial Therapy with Once-Weekly Secnidazole Granules to Prevent Recurrent Bacterial Vaginosis; a Pilot Study
Lupin Pharmaceuticals, Inc.

ABOUT THIS RESEARCH

You are being asked to participate in a research study. Scientists do research to answer important questions which might help change or improve the way we do things in the future.

This consent form will give you information about this study to help you decide whether you want to participate. It is your choice whether or not you want to be in this research study. Please read this form, and ask any questions you have, before agreeing to be in this study.

WHY IS THIS STUDY BEING DONE?

Bacterial vaginosis (BV) is the most common cause of vaginal symptoms in women in the United States. Many women will have repeat episodes of BV after receiving standard treatment and there are limited options for treating women with recurrent BV.

The purpose of this study is to test the effectiveness of a medication called "Secnidazole" to treat recurrent BV. Secnidazole is approved for one-time use in acute BV. In this study, the drug will be used for recurrent BV, and given weekly for 18 weeks.

We are asking you if you want to be in this study because you currently have symptoms of BV, have a history of at least two previous episodes of BV in the past year, and are 18-50 years old.

The study is being conducted by Dr. Chemen Neal at Indiana University Department of Obstetrics and Gynecology. It is funded by Lupin Pharmaceuticals, Inc who manufactures secnidazole.

HOW MANY PEOPLE WILL TAKE PART?

You will be one of 50 participants taking part in this study.

WHAT WILL HAPPEN DURING THE STUDY?

All visits will occur at IU Health Coleman Center

Visit 1 – Enrollment - Baseline Assessment

- For research purposes the study team will collect information about you from your medical records.
- You will answer questions about your symptoms.
- We will perform a symptom assessment, pelvic exam, and obtain vaginal swabs to evaluate your symptoms. The pelvic exam of the vagina is like pelvic examinations performed clinically at most annual gynecologic examinations. The pelvic exam will take about 2 minutes.

- You will have a basic neurological exam. The neurological exam will take about 2 minutes. The neurological exam will take about 2 minutes. Cranial nerves 2-12 will be evaluated (nerves that are in your face and head), and your arm and leg strength and reflexes will be tested.
- We will perform STI testing for gonorrhea/chlamydia/trichomonas.
- We will perform a urine pregnancy test. If you are pregnant, you will not continue with study drug.
- We will provide you with secnidazole and you will be instructed in the use of the secnidazole granules by trained study personnel or your medical provider. You will take secnidazole orally, once a week - initially for 2 weeks.
- You will be asked to attend follow-up clinic visits throughout the study to undergo additional pelvic exams, assess your symptoms and evaluate your vaginal discharge, vaginal irritation, bleeding, redness, or itching as well as medication intake, tolerance, and any potential side effects.
- Each study visit will last about 30 minutes to 1 hour.
- Any testing performed that is part of the standard evaluation of your symptoms will be billed to you and/or your insurance. Study related testing and examinations will not be charged to you. Your provider will explain which parts of your examination are standard or study related.

Visit 2 – 3 to 5 days after the 2-week treatment period

- You will attend a follow-up visit, where we will again assess your symptoms, perform a pelvic exam, and evaluate your symptoms.
- You will have a basic neurological exam at follow-up clinic visits.
- You will also complete a questionnaire that asks about symptoms, the use of contraception, and any side effects you may have experienced.
- If we find that secnidazole is not treating your symptoms of bacterial vaginosis at this visit or subsequent follow-up visits, your participation in the study will be considered complete and you will be placed on standard therapy for recurrent BV.
- If you show signs of resolution, you will continue to take secnidazole once a week up until week 16.

Visit 3 through 6 – Weeks 6, 10, 14, and 18

- Every 4 weeks up until Week 16, you will attend follow-up visits to assess your symptoms, and make sure you are taking the study drug.

Visit 7 and 8 – Weeks 22 and 30

- If you remain without recurrence during the 16-week treatment phase, you will be followed for an additional 12 weeks (about 3 months) off therapy with follow-up visits at weeks 22 and 30.
- You will be followed for up to 30 weeks (about 7 months) total if you remain symptom free.

If you participate in this study, we may learn things about you from the study procedures that could be important or interesting to you. Depending on the information, you might need to meet with professionals with expertise to help you decide what to do with the information. We do not have money or funds available to cover the costs of any follow-up consultations or actions. We will share the following information with you:

- Any information that might be immediately critical to your health will be shared with you or your health care provider.

WHAT ARE THE RISKS OF TAKING PART IN THE STUDY?

While participating in the study, the risks, side effects, and/or discomforts include:

- A risk of completing the survey is being uncomfortable answering the questions. You can skip any questions that make you uncomfortable or that you do not want to answer.
- There is a risk someone outside the study team could get access to your research or medical information from this study. More information about how we will protect your information to reduce this risk is described later in this document.
- The risks of a speculum pelvic exam include pain and discomfort.
- Previous trial data shows that 30% of all treated individuals will report a side effect to secnidazole. The side effects associated with taking secnidazole include (in parenthesis are the percentage of individuals who reported that side effect):
    - Vaginal candida infection (9.6%)
    - Headache (3.6%)
    - Nausea (3.6%)
    - Temporary loss of taste (3.4%)
    - Vomiting (2.5%)
    - Diarrhea (2.5%)
    - Abdominal pain (2%)
    - Vaginal itching (2%)
- Prior clinical studies of secnidazole reported mild prolongation of QTc (a portion of the heartbeat) after single 2g or 6g doses. While this was found to be clinically insignificant, it is still a symptom that you might encounter.
- Animal trials in rats and dogs demonstrated neurological adverse events in toxicity studies. No significant accumulation of the drug is expected in humans when treated weekly for 18 weeks, but multi-dose regimens of secnidazole have not been studied in humans.
- You should avoid pregnancy during the active treatment period of participation in this study since secnidazole has not been studied in pregnancy. Effective contraception includes condoms, implants, intrauterine devices, injectable medications, pills, and patches.
- Animal trials in mice and rats have demonstrated cancer-causing effects with nitroimidazole derivatives (chemicals similar to secnidazole) after lifetime exposure and when used at very high doses (1.4 times the normal human dose). Up to the present, no carcinogenic effects have been observed in humans. It is unclear if the rodent studies indicate risks to patients taking secnidazole.
- Alcoholic beverages and preparations containing ethanol or propylene glycol should be avoided during secnidazole therapy and for 2 days after treatment is stopped. Nausea,

vomiting, diarrhea, abdominal pain, dizziness, and headache have been reported when secnidazole was taken at the same time as alcohol.
- Whenever an antibiotic is used, there is potential for the development of drug-resistant bacteria. Secnidazole should only be used when an infection is proven or strongly suspected.

To reduce the potential for these risks the following measures will be employed:
- While completing the survey, you can tell the researcher that you feel uncomfortable or that you do not want to answer a particular question.
- Speculum exams will be completed by experienced providers and, whenever possible, it will be collected at a time when you are already having a speculum exam.
- While you are receiving secnidazole, you will be questioned weekly about side effects, and you will be monitored utilizing a speculum exam.

There also may be other side effects that we cannot predict. If you become pregnant while you are participating in this study, this may include risks to your unborn baby.

WHO WILL PAY FOR MY TREATMENT IF I AM INJURED?

If you are injured as a result of participating in this study necessary medical treatment will be provided to you and billed as part of your medical expenses. Costs not covered by your health care insurer will be your responsibility. Also, it is your responsibility to determine the extent of your health care coverage. No money or funds are set aside to pay for these types of injuries. However, you are not giving up any legal rights or benefits to which you are otherwise entitled by signing this Informed Consent form.

WHAT ARE THE BENEFITS OF TAKING PART IN THE STUDY?

Participating in this study may reduce the recurrence of your bacterial vaginosis. However, we do not know for sure. We are doing this research study to find out if this treatment helps or not.

WILL I BE PAID FOR PARTICIPATION?

You will be compensated $30 for each study visit you attend. If you are eligible after visit 2 you could attend up to 8 study visits for a total of $240. If you develop symptoms of bacterial vaginosis at visits 2 through 6 you will not be able to continue with study visits.

WILL IT COST ME ANYTHING TO PARTICIPATE?

There is no cost to you for taking part in this study. Any testing performed that is part of the standard evaluation of your symptoms will be billed to you and/or your insurance. Study related testing and examinations will not be charged to you. Your provider will explain which parts of your examination are standard or study related.

WHAT ARE THE OTHER TREATMENT OPTIONS?

There may be other options for treatment of your bacterial vaginosis. There are other antibiotic therapies and treatment durations available to you should you choose to not participate in this research study.

HOW WILL MY INFORMATION AND SPECIMENS BE USED?

The following individuals and organizations may receive or use your identifiable health information:

- The researchers and research staff conducting the study
- The Institutional Review Boards (IRB) or its designees that review this study
- Indiana University
- US or foreign governments or agencies as required by law
- Data safety monitoring boards and others authorized to monitor the conduct of the study
- The following research sponsors: Lupin Pharmaceuticals, Inc.
- State or Federal agencies with research oversight responsibilities, including but not limited to:
    - The United States Food and Drug Administration (FDA)

The study sponsor, Lupin Pharmaceuticals, Inc, will access research information to monitor safety and progress of the study.

Information and specimens collected for this study may be used for other research studies or shared with other researchers for future research. If this happens, information that could identify you, such as your name and other identifiers, will be removed before any information or specimens are shared. Since identifying information will be removed, we will not ask for your additional consent.

A description of this clinical trial will be available on ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

HOW WILL MY INFORMATION BE PROTECTED?

Every effort will be made to keep your personal information confidential, but we cannot guarantee absolute confidentiality. No information which could identify you will be shared in publications about this study. Your personal information may be shared outside the research study if required by law and/or to individuals or organizations that oversee the conduct of research studies.

WHAT WILL YOU DO WITH MY GENETIC INFORMATION?

We will not use the specimens collected as a part of this study for whole genome sequencing, which involves mapping all of your DNA.

WHO SHOULD I CALL WITH QUESTIONS OR PROBLEMS?

For questions about the study or a research-related injury, contact the researcher, Dr. Chemen Neal, at 317-948-3148. After hours, please call 317-944-8231.

In the event of an emergency, please call 911.

If you are unable to reach the investigator at the above number(s) in an emergency, you may contact the University Hospital pharmacy at 317-944-0362 and ask them to page the IDS pharmacist on call.

For questions about your rights as a research participant, to discuss problems, complaints, or concerns about a research study, or to obtain information or to offer input, please contact the IU Human Research Protection Program office at 800-696-2949 or at irb@iu.edu.

WHAT IF I DO NOT PARTICIPATE OR CHANGE MY MIND?

After reviewing this form and having your questions answered, you may decide to sign this form and participate in the study. Or you may choose not to participate in the study. This decision is up to you. If you choose not to participate in this study or change your mind after signing this document, it will not affect your usual medical care or treatment or relationship with Indiana University or University Hospital.

If you change your mind and decide to leave the study in the future, the study team will help you withdraw from the study safely. If you withdraw from the study, you may experience a recurrence of BV symptoms. If you decide to withdraw, notify Dr. Neal via phone or at your next visit to determine if additional or alternative treatment will be necessary. You may also contact the study team at 317-948-3148 or in writing at 550 University Blvd Ste 2440, Indianapolis, IN 46202.

The researchers may stop your participation in the study even if you do not want to stop if you experience unexpected side effects such as an allergic reaction or other adverse reaction.

PARTICIPANT'S CONSENT

In consideration of all the above, I agree to participate in this research study. I will be given a copy of this document to keep for my records.

Participant's Printed Name **Date**	**Printed Name of Person Obtaining Consent** **Date**
Participant's Signature	**Signature of Person Obtaining Consent**