The Cleveland Clinic Foundation
Consent to Participate in a Research Study

Study title: A randomized controlled trial to determine the effect of gabapentin enacarbil on opioid consumption and pain scores in patients having hip and knee arthroplasties with spinal anesthesia.

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Main Campus Site Director:	Loran Mounir Soliman, M.D.	Tel: 216-445-4868
Sponsor:	XenoPort, Inc	Tel: 408-616-7200

Carefully review this consent document. The purpose of a consent document is to provide you with the information to help you decide whether you wish to participate in research. Your decision is completely voluntary and will not affect your medical care if you chose not to participate. It is important for you to ask questions and understand the risks, benefits and alternatives.

You are being invited to participate in a research study. A research study is designed to answer specific questions about new ways to prevent, detect, and treat disease. Being in a research study is different from being a patient. The purpose of this document is to provide a written summary of the discussion and exchange of research information you had with the research team. It is also for use as a reference during the study.

Please note:
· **You are being asked to participate in a research study.**
· **Ask as many questions as needed so you can make an informed decision.**
· **Carefully consider the risks, benefits, and alternatives of the research.**
· **Your decision to participate is completely voluntary and will have no effect on the quality of your medical care if you choose not to participate. You can also withdraw from the study at any time.**

This research study has been approved by the Institutional Review Board (IRB). The IRB is a committee that reviews human research studies to ensure the safety and welfare of research volunteers are protected in accordance with federal human subject regulations and ethical principles.

Why Are You Being Asked to Take Part In This Research?

You are being invited to take part in this research study because you are having elective hip and knee surgery.

Why is the research study being done?

Opioids are effective analgesics (pain relievers), but cause side effects including sedation, respiratory depression, low blood pressure, nausea, and constipation. Gabapentin enacarbil, which is a FDA approved drug for post herpetic neuralgia (nerve pain related to shingles) and

restless leg syndrome, may decrease your need for narcotics and thus decrease the risk of side effects. The main purpose of this study is to determine if gabapentin enacarbil decreases opioid consumption and pain after surgery. We will also evaluate the cost effectiveness of gabapentin enacarbil.

How Many People Will Take Part In The Study?

About 100 patients will take part in this study at the Fairview Hospital and Cleveland Clinic Main Campus.

What is involved if you decide to take part in this research study?

If you agree to be in this study, you will be asked to sign this consent form. The following assessments will be carried out:

Screening Visit (up to 14 days before surgery)

- Your eligibility for the study will be determined
- Full details of the study will be discussed with you and if you agree to take part you will be asked to sign a Consent Form.
- Medical History
- A physical examination
- Vital signs
- Pain will be assessed by the Brief Pain inventory and numerical rating scores
- Randomized, like flipping a coin, to receive either:
  - Gabapentin enacarbil (Gen) 600 mg twice per day for 5 days or
  - Placebo (inactive substance) twice per day for 5 days.

Neither you nor your physician will know if you are assigned to study drug or placebo. Regardless of study assignment, both groups will receive standard pain management medications and sedation during surgery.

Two Days prior to Surgery

- You will receive a phone call to remind you to start taking your medication the next morning

One day prior to surgery

- Take GEn 600 mg or placebo 600 mg twice a day with meals.

Day of Surgery

- Medical History
- Social History
- Demographic data such as height, weight, age, gender and self-declared ethnicity
- Your risk of nausea and vomiting will be assessed
- Two hours prior to the surgery you will be asked to take GEn 600 mg or placebo 600 mg with sips of water. Any pain you might experience after your surgery will be properly addressed and treated.

- The first hour after surgery, your pain will be assessed every 15 minutes using a numerical rating score
- 6 hours after the completion of surgery, you will receive GEn 600 mg or placebo 600 mg
- If you are sent home after surgery, you will be given 6 GEn 600mg or placebo 600mg pills to take home with you along with instructions.

First Day after Surgery (as long as you are hospitalized)

- Your pain will be assessed in the morning using a numerical rating score
- You will evaluate the quality of your recovery by answering a questionnaire
- You will receive GEn 600 mg or placebo 600 mg twice a day with meals.

Second Day after Surgery (as long as you are hospitalized)

- Your pain will be assessed in the morning using a numerical rating score
- You will receive GEn 600 mg or placebo 600 mg twice a day with meals
- If you are discharged on the second day a follow-up phone call will be made to you for each second and third day after surgery

Third Day after Surgery (as long as you are hospitalized)

- Your pain will be assessed in the morning using a numerical rating score
- You will receive GEn 600 mg or placebo 600 mg twice a day with meals
- If you are discharged on the third day after surgery a follow-up phone call will be made on the third day after surgery

Three Months after Surgery

- You will receive a phone call to follow-up with possible pain or discomfort you may be feeling.

What are the alternatives to participation in the research study?

You may agree to participate or decline. If you decline you will receive usual care for your pain after surgery.

What are the risks of participating in the research study?

Gabapentin enacarbil should not be used in patients with known hypersensitivity to gabapentin or gabapentinoids. Gabapentin enacarbil should be used with caution in patients with the following conditions: renal impairment or active renal disease, having current depression or currently on any prescribed anti-depressant medication or seizure disorder within the last one-year or taking medications for seizures. The most common adverse reactions in adult patients treated with gabapentin enacarbil are sleepiness, sedation, and dizziness, loss of coordination, or blurred vision. You must not take any other medications containing gabapentin or gabapentinoids (e.g. Lyrica, Horizant, Neurontin or Gralise) while on this study.

Unforeseeable risks:

There may be risks or side effects related to the study drug that are unknown at this time. You will be notified of any significant new findings that become known that may affect your willingness to continue in the study.

Pregnant women, fertile females/males:

There may be unforeseen risks to an unborn child associated with your taking gabapentin enacarbil.
Gabapentin enacarbil is Pregnancy Category C; There are no studies of gabapentin enacarbil in pregnant women; However, epidemiological data on oral gabapentin use in pregnant women show no increased risk of major congenital malformations. Animal reproduction studies have not been conducted with gabapentin enacarbil, and it is not known whether gabapentin enacarbil can cause fetal harm when administered to a pregnant woman. Pregnancy test will be performed on all women of child-bearing potential to rule out pregnancy before undergoing elective surgery.

What are possible benefits of participating in the research?

There is no personal benefit to you by participating in this research study, but knowledge gained may benefit other patients, society, or science.

Are there any costs to you if you participate in this study?

There are no additional costs to you for participation in this research study. The cost for routine tests and services that would normally be performed even if you do not participate in the study will be billed to you or your insurance provider. The study drug (Gabapentin enacarbil) will be provided by XenoPort Inc..

Are there any payments to you if you participate in this study?

You will not be compensated for your participation in this research study.

What will happen if you are injured as a result of taking part in the research?

In the event you are injured as a result of participation in this research, medical care is available to you. The cost of such medical care will be billed to you or your insurance company. There are no plans to provide compensation for lost wages, direct or indirect losses. The Cleveland Clinic will not voluntarily provide compensation for research related injury. You are not waiving any legal rights by signing this form.

Further information about research related injury is available by contacting the institutional review board at 216-444-2924.

What will happen to your information that is collected for this research?

If you volunteer to participate in this research, your protected health information (PHI) that identifies you will be used or disclosed to Sabry Ayad, M.D., Loran Mounir Soliman, M.D. and the research staff at Cleveland Clinic for the purposes of this research. Any information obtained in connection with this research study that can identify you will remain confidential. Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except required by law.

All participants will be given a study code number. All information about you that is collected for the study will be labeled with this number, not your name or hospital number. The key to the code will be stored separately to your information.

The PHI that we may use or disclose (release) for this research may include your name, address, phone number, date of birth and information from your medical records.

In addition to the investigators and research staff listed above, your PHI may be looked at by other groups involved with the study such as the Cleveland Clinic Institutional Review Board, Xenoport, Inc.

Records are collected and stored either in folders (for paper records) or put onto a secure computer, which can only be accessed by the researchers. All written data will be stored in a locked filing cabinet in a locked room. Only the researchers will have access to stored written or electronic data. Information collected from participants will be kept for 15 years after which it will be destroyed.

Once your personal health information is released it may be re-disclosed and no longer protected by privacy laws.

Fairview participants may stop the uses and disclosures of your information at any time by writing to Sabry Ayad, M.D. Chairman, Department of Anesthesiology, Fairview Hospital, Cleveland Clinic 18101 Lorain Avenue, Cleveland, OH 44111, Tel: 216-476-7052 Cleveland Clinic Main Campus participants may stop the uses and disclosures of your information at any time by writing to Loran Mounir Soliman 9500 Euclid Ave., E31 Cleveland, OH 44195 216-445-4868. Your participation in the research will stop, but any information previously recorded about you cannot be removed from the records and will continue to be used as part of this research. Also, any information already disclosed outside the Cleveland Clinic cannot be retrieved. This will not affect your rights to treatment or benefits outside the research study.

The Cleveland Clinic will not use your information collected in this study for another research purpose without your written permission unless the Cleveland Clinic Institutional Review Board (IRB) assures your privacy and confidentiality is protected. The IRB is a committee whose job it is to protect the safety and welfare of research subjects.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission.

Information about your participation in this research study will be recorded in your health records.

You have the right to request access to your information collected and stored by the research team. You also have the right to request that any information with which you disagree be corrected. Contact the study team member named at the end of this document if you would like to access your information.

By signing this informed consent form, you are authorizing such access to your research and medical record information. If you choose not to sign this consent form, you will not be able to participate in this research study. This Authorization does not have an expiration date.

Who do you call if you have any questions or problems?

If you are a Fairview Hospital patient and have any questions, you can ask the Principal Investigator Sabry Ayad, M.D, at 216-476-7052.

If you are a Fairview patient, you should contact the page operator at (216) 476-7000 or toll free at 800-223-2273, and ask for Sabry Ayad, M.D.

If you are a Cleveland Clinic Main Campus patient and have any questions, you can ask the Principal Investigator, Loran Mounir Soliman, M.D. at 216-445-4868.

If you are a Cleveland Clinic Main Campus patient, you should contact the page operator at 216-444-2200 and ask for Lorain Mounir Soliman, M.D.

If you have any questions about your rights as a research subject, you may contact the Institutional Review Board (IRB) at Cleveland Clinic IRB 216-444-2924.

What are your rights as a research participant?

Participation in this research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the study at any time.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with the Cleveland Clinic.

In the event new information becomes available, that may affect the risks or benefits associated with this study or your willingness to participate in it, you will be notified so that you can decide whether or not to continue participating.

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

Statement of Participant

I have read and have had verbally explained to me the above information and have had all my questions answered to my satisfaction. I understand that my participation is voluntary and that I may stop my participation in the study at any time. Signing this form does not waive any of my legal rights. I understand that a copy of this consent will be provided to me. By signing below, I agree to take part in this research study.

_____
Printed name of Participant

_____
Participant Signature

_____
Date

Statement of Person Conducting Informed Consent Discussion

I have discussed the information contained in this document with the participant and it is my opinion that the participant understands the risks, benefits, alternatives and procedures involved with this research study.

_____
Printed name of person obtaining consent

_____
Signature of person obtaining consent

_____
Date

Cleveland Clinic

AUTHORIZATION FOR THE RELEASE OF MEDICAL INFORMATION FROM OTHER HEALTHCARE FACILITIES

Name:_____ SS#:_____

CC#:_____ Date of Birth: _____/_____/_____

Telephone #:_____ Address:_____

City:_____ State:_____ Zip:_____

Name of Healthcare Facility from which Records are Requested:

_____

Address: _____

Street: _____

City: _____ State:_____ Zip:_____

Dates of Treatment Requested: _____

Reason for Disclosure: _____

MAIL INFORMATION TO: **OR** **MAIL INFORMATION TO :**

Release Medical Information to: (please check one box and provide needed information)

☐ Cleveland Clinic
c/o _____ Mail Code:_____
9500 Euclid Avenue
Cleveland, OH 44195
Phone: _____
Fax: _____

Department: _____

☐ _____
_____
_____
_____

I hereby authorize Cleveland Clinic to obtain the health information indicated below that is contained in my patient records to the Recipient named above. **I understand and acknowledge that this may include treatment for physical and mental illness, alcohol/drug abuse, and or HIV/AIDS test results or diagnoses. This authorization does not include permission to release outpatient Psychotherapy Notes. The release of Psychotherapy Notes requires a separate authorization. Psychotherapy Notes are defined as notes that document private, joint, group, or family counseling sessions that are separated from the rest of a patient's medical record.**

	Emergency Department Reports		Pathology Reports
	Discharge Summary		Laboratory Reports
	History & Physical		Radiology Reports
	EKGs		Operative Reports
	Physical/Occupational Therapy Reports		Other (Specify)

This consent is subject to revocation at any time except to the extent the action has been taken thereon. **This authorization and consent will expire one year from the date of authorization written below.**

Your health care (or payment for care) will not be affected by whether or not you sign this authorization. Once your health care information is released, redisclosure of your health care information by the Recipient may no longer be protected by law.

_____/_____ _____/_____/_____

*Signature of Patient/Patient's Personal Representative*** *Printed Name* *Date Signed*

_____

Relationship if not Patient

***If other than the patient's signature, a copy of legal paperwork verifying the patient's personal representative MUST accompany the request (i.e. court appointed guardian, durable power of attorney for health care). For a deceased patient: A death certificate coupled with executor or administrator of estate paperwork must accompany authorization. Exception: parent signing for patient under the age of 18.*

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