UNIVERSITY OF PENNSYLVANIA
RESEARCH PARTICIPANT
INFORMED CONSENT AND HIPAA AUTHORIZATION FORM

Protocol Title:	**C**omparison of **A**pixaban ve**r**sus **E**noxaparin for VTE Prevention after Radical Cystectomy (**CARE**)
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Research Study Summary for Potential Participants

You are being invited to participate in a research study. Your participation is voluntary, and you should only participate if you completely understand what the study requires and what the risks of participation are. You should ask the study team any questions you have related to participating before agreeing to join the study. If you have any questions about your rights as a human research participant at any time before, during or after participation, please contact the Institutional Review Board (IRB) at (215) 898-2614 for assistance.

The research study is being conducted to better understand the experience of taking blood thinning medications at home after bladder removal surgery. There are two types of blood thinner that can be prescribed after bladder removal surgery. One is called enoxaparin; it is taken by self-injection once daily. The other is called apixaban; it is taken orally twice daily. Patients are instructed to take whatever drug they are prescribed until the 30th day after surgery. It is known that taking either of these blood thinners for this period of time after surgery has clinical benefit by preventing harmful blood clots and the benefit is thought to be equal between the two drugs. However, patients frequently voice frustrations with these medications, including difficulty remembering to take them, administer them, and/or pay for them. These issues may discourage providers from prescribing blood thinners, or patients from taking them. Therefore, we would like to determine definitively which of the two blood thinners is more tolerable, more cost friendly, and which leads to higher adherence rates.

If you agree to join the study, you will be asked to complete the following research procedures:

- Sign consent form
- Complete the Demographic Questionnaire either in person, over the phone, or via emailed link

- Randomization to either enoxaparin or apixaban after bladder removal surgery. Randomization means neither you nor your study doctor will get a choice as to which treatment arm you will get. That assignment will be random, like flipping a coin.
- Your medical chart will be reviewed for additional demographic information and technical details about your surgery
- Speak on the phone with a member of the research team around 30 days after surgery. The phone conversation will consist of a few short questionnaires. If you prefer, most of these questionnaires can instead be emailed to you securely, however you will still need to answer the initial phone call and indicate your preference.
- Medication Counting: keep the entire medication supply you are given (ie do not throw any unused medication away) until your phone call at 30 days, at which point you will be asked to count the remaining pills/vials of medication
- Complete one more short questionnaire either over the phone or via email at 90 days after your surgery

Your participation will last until 90 days after your surgery.

There is no anticipated benefit from participating. The most common risks of participation are the risks of the medications given, which are a routine part of care regardless of participation in this trial. These risks are further explained in the drug labels. The most common risk is that of serious bleeding. Enoxaparin may also be associated with low platelet counts, diarrhea, nausea, and liver dysfunction in rare cases.

If you choose not to participate you will still undergo bladder removal surgery as planned. You will still be given a prescription for a blood thinner prior to discharge and instructed to self-administer it until 30 days after surgery as this is the standard of care with known benefit.

Please note that there are other factors to consider before agreeing to participate such as additional procedures, use of your personal information, costs, and other possible risks not discussed here. If you are interested in participating, a member of the study team will review the full information with you. You are free to decline or stop participation at any time during or after the initial consenting process.

Why am I being asked to volunteer?

You are being invited to participate in a research study because you are a patient planning to undergo cystectomy (surgical removal of bladder) with use of low dose blood thinner at home afterwards (standard care).

Your doctor may be an investigator in this research study. You do not have to participate in any research study offered by your doctor. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled. You may also decide to discuss the study with your family, friends, or family doctor. Being in a

research study is different from being a patient. As an investigator, your doctor is interested both in your clinical welfare and in the conduct of this study.

If you decide to participate, you will be asked to sign this form.

What is the purpose of this research study?

The purpose of this study is to better understand the experience of patients who have to take blood thinners at home themselves after bladder removal surgery. When the bladder is removed for cancer this is a major operation with several associated risks, one of which is an increased risk of blood clots during the recovery period after surgery. Developing a blood clot, if not fatal, can lead to many months of taking high dose blood thinners, which have associated risks of their own including excessive bleeding, needing follow-up visits, and high costs of the medication. In order to decrease the changes of forming a blood clot, Urologists have started proactively sending patients home on a low dose of blood thinner. Patients are told to take this blood thinner until the 30th day after their surgery. Patients can take this blood thinner themselves or arrange for a family member or hired caregiver to help them with it. Studies have shown that this practice does significantly decrease clots.

However, despite evidence showing the benefit of these at-home blood thinners, not all patients are given prescriptions for blood thinners. Part of the reason why is because one of the most commonly used blood thinners, enoxaparin, is disliked by patients due to the need to administer it by self-injection. Some surgeons have therefore switched to using another blood thinner, apixaban, which is a pill that can be taken orally. While this seems more appealing, there are still possible issues with using apixaban, such as its more frequent dosing and higher price.

Both enoxaparin and apixaban are acceptable choices for a blood thinner at home; neither is experimental. Since the two blood thinners have never been directly compared (“head-to-head”) we are proposing a study where patients are randomized to receive either enoxaparin or apixaban prior to going home from surgery. We will then compare their adherence to the medication, their financial costs, and their overall satisfaction/dislike of the experience of taking the blood thinner at home. This will help future Urologists make the best choice for patients when prescribing them a blood thinner to take at home after bladder removal surgery.

How long will I be in the study?

You will technically be enrolled in this study from the day of consent until 90 days after your bladder removal surgery. During this time period you will be participating actively during one phone call around 30 days after surgery, and a second phone call around 90 days after surgery

What am I being asked to do?

If you agree to join the study, you will be asked to complete the following research procedures for the purpose of research:

- Sign consent form
- Complete the Demographic Questionnaire either in person or over the phone
- Randomization to one of the two blood thinners: either enoxaparin or apixaban. Randomization will occur after surgery but before discharge. Randomization means neither you nor your study doctor will get a choice as to which treatment arm you will get. That assignment will be random, like flipping a coin
- Your medical chart will be reviewed for additional demographic information and technical details of your surgery
- Speak on the phone with a member of the research team around 30 days after surgery. The phone conversation will consist of a few short questionnaires. If you prefer, we can email you a link to complete these questionnaires on the secure research platform REDCap rather than over the phone, however you will still need to answer the initial phone call and indicate your preference. These questionnaires will ask about what was challenging about being at home on one of the blood thinners, what you may have liked or disliked about them, and how you handled the logistics of taking them.
- Medication Counting: keep the entire medication supply you are given (ie do not throw any unused medication away) until your phone call at 30 days, at which point you will be asked to count the remaining pills/vials of medication
- Complete one more short questionnaire about the financial burdens of your cancer care either over the phone or via email at 90 days after your surgery

What are the possible risks or discomforts?

Risks and discomforts are minimal. All are associated with the drugs, which are standard care, and listed on drug labels. The most common risk is that of serious bleeding. Enoxaparin may also be associated with low platelet counts, diarrhea, nausea, and liver dysfunction in rare cases. During the study, information about you will be recorded. There is a risk of breach of confidentiality and privacy. The research team will take precautions to make sure your privacy is maintained. We will use commercial-grade encryption to protect your information. Your personal information will only be used by study team members who have been trained to use secure protocols to maintain the privacy of your data. Whenever possible, data will be de-identified to protect your privacy.

What if new information becomes available about the study?

During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

What are the possible benefits of the study?

You are not expected to get any direct benefit from being in this research study. It is expected that this knowledge could help inform providers about patient comfort and feasibility using these medications at home after surgery.

What other choices do I have if I do not participate?

If you choose not to participate you will still undergo bladder removal surgery as planned. You will still be given a prescription for one of these two blood thinners prior to discharge and instructed to self-administer it until 30 days after surgery as this is the standard of care with known benefit.. You may further discuss the option of not participating with your personal physician.

Will I be paid for being in this study?

Yes, you will be compensated $20 at the completion of the study. A Greenphire ClinCard will be used to pay you. This is a debit card that can be virtual or physically handed to you. If you withdraw from the study or are discontinued prior to completing the 90 day phone call visit you will not receive the $20 compensation.

Will I have to pay for anything?

The blood thinners are not directly provided by the study. Rather, prescriptions for the blood thinners are given like they would be if you were not in the study. Your insurance will be billed to help pay for them in the usual way, however you may still be responsible for some drug costs. These costs will be the same as if you were not participating in this study.

You are still responsible for any deductibles or applicable co-pays for all other aspects of your care including office visits, scans and blood work. Please talk to your doctor and study team about putting you in touch with a financial counselor to determine exactly what the deductible and co-pay will be for you; this is highly variable depending on your type of insurance.

What happens if I am injured from being in the study?

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury. If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. You do not give up your legal rights by signing this form.

If you think you have been injured as a result of taking part in this research study, tell the person in charge of the research study as soon as possible. The researcher's name and phone number are listed in the consent form.

When is the Study over? Can I leave the Study before it ends?

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped at any time by your

physician, the study Sponsor, or the Food and Drug Administration (FDA) without your consent because:

- The Primary Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The Sponsor, the study Principal Investigator, or the Food and Drug Administration (FDA) has decided to stop the study.

If you decide to participate, you are free to leave the study at any time. You may do this by contacting the investigator noted on page one of this form. Withdrawal will not interfere with your future care.

If you decide to stop participating in the study, we encourage you to talk to your doctor first. It is important to tell the doctor if you are thinking about stopping so any risks to you can be minimized. A final study visit may be requested to ensure your safety.

How will my personal information be protected during the study?

We will do our best to make sure that the personal information obtained during the course of this research study will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. The Institutional Review Board (IRB) at the University of Pennsylvania will have access to your records. If this study is being overseen by the Food and Drug Administration (FDA), they may review your research records.

The confidentiality of your information will be protected in the following way during the study. Data will be stored, managed, and analyzed on a secure, encrypted server behind the University of Pennsylvania Health System (UPHS) firewall. Data from the questionnaires and data from your medical chart will be captured directly through the HIPAA complaint REDCap service housed at the University of Pennsylvania. Access to REDCap is password protected and will be limited only to study personnel.

Will information about this study be available to the public?

A description of this clinical trial will be available on www.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.

What may happen to my information collected on this study?

Future Use of Data

Your coded or identifiable information will be stored for future research purposes. Future researchers may receive information that could identify you. This can be done without again seeking your consent in the future, as permitted by law. The future use of your information only applies to the information collected on this study.

The following identifiers will be retained with your information: name, date of birth, address, telephone number, email, MRN, medical comorbidities, and sex/gender.

Your information may be stored and used for future research purposes for an indefinite amount of time.

There are no plans to tell you about any of the specific research that will be done.

We will not share your identifiable information with other research institutions or pharmaceutical, device, or biotechnology companies.

We will not follow up with you to tell you about the specific research that will be done. It is possible that you may have chosen not to participate in these future research studies, had you been approached for participation.

There is a risk of breach of confidentiality (unintentional release of your information). We will do our best to make sure that this doesn't happen. However, we cannot guarantee total privacy. We will protect your confidentiality during storage and sharing by collecting data directly into REDCap, which is a password-protected software accessible only to the study team. REDCap is housed on the secure, encrypted server behind the University of Pennsylvania Health System firewall.

You will likely not directly benefit from future research with your information. Research with your identifiable information may help others by improving our understanding of health and disease, improving healthcare and making safer or more effective medical therapies, and developing new scientific knowledge.

If you have questions about the storage of your information, or have changed your mind, you can contact the research team at 215-615-3780.

Electronic Medical Record and Release of Study Related Information

What is an Electronic Medical Record?

An Electronic Medical Record (EMR) is an electronic version of your medical chart within a health system. An EMR is simply a computerized version of a paper medical record.

If you have never received care within Penn Medicine and are participating in a University of Pennsylvania research study that uses Penn Medicine healthcare related services, an EMR will be created for you for the purpose of maintaining any information produced from your participation. The creation of this EMR is a requirement of your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). If you have been a patient at Penn

Medicine in the past, information from your research participation will be added to your existing medical record.

What may be placed in the EMR?
Information related to your participation in the research (e.g., laboratory tests, notes from your physician, imaging studies, and clinical procedures, etc.) will be placed in your EMR maintained by Penn Medicine.

Once placed in your EMR your information may be accessible to appropriate Penn Medicine workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by Penn Medicine to be appropriate to have access to your EMR (e.g. Health Insurance Company, disability provider, etc.).

Penn Medicine also participates in automated information sharing through Health Information Exchanges (HIEs). HIEs securely share parts of your electronic health record, including research information, with other healthcare organizations involved in your care. This information is shared to improve the quality, safety and efficiency of your healthcare. To request that your health information not be shared through HIEs, please call 215-662-4484.

Will I, as a participant, have access to research related information within the EMR?
The 21st Century Cures Act requires healthcare institutions to allow patients increased access to their electronic medical record. As part of your participation in this research, you will have access to research related information within your EMR through Penn Medicine's patient portal – called MyPennMedicine (MPM).

Some information specific to this clinical research study may be shared with you in a delayed manner, shared with you at the end of the study, or not shared with you. Not sharing or delaying certain research information within your EMR may be necessary to protect the integrity of the trial results or for other reasons.

Will I receive the results of research testing that may be relevant to my health?
Many of tests done in research studies are only for research and have no clear impact on your healthcare. Research results for this study will not be returned to you because they would not be relevant to your healthcare.

What information about me may be collected, used or shared with others?
- Name
- Birth date
- Address
- Telephone number

- Electronic mail addresses
- Medical record number
- Medical comorbidities
- Sex assigned at birth, gender

Why is my information being used?

Your information is used by the research team to contact you during the study. Your information and results of tests and procedures are used to:

- do the research
- oversee the research
- to see if the research was done right
- to evaluate and manage research functions.

Where may my information be stored?

Information related to your participation in clinical research will be contained in a clinical trial management system (CTMS). A clinical trial management system (CTMS) is used to register your information as a participant in a study. This allows for your research data to be entered and stored for the purposes of study operational and financial applications and other activities required as part of the conduct of the research. Once placed in the CTMS your information may be accessible to other authorized personnel at Penn Medicine that support research operations. Your information may be held in other research databases.

Who may use and share information about me?

The following individuals may use or share your information for this research study:

- The investigator for the study and the study team
- Other authorized personnel at Penn Medicine and the University of Pennsylvania, including offices that support research operations
- Other research personnel with access to the databases for research and/or study coordination and as otherwise approved by the IRB

Who, outside of Penn Medicine, might receive my information?

<u>Partner Universities</u>

- Vanderbilt Medical Center

<u>Oversight organizations</u>

- The U. S. Office of Human Research Protections (OHRP)

Once your personal health information is disclosed to others outside Penn Medicine, it may no longer be covered by federal privacy protection regulations.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to Penn Medicine procedures developed to protect your privacy.

How long may Penn Medicine use or disclose my personal health information?

Your authorization for use of your personal health information for this specific study does not expire.

However, Penn Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization
- The University of Pennsylvania's Institutional Review Board grants permission
- As permitted by law

Can I change my mind about giving permission for use of my information?

Yes. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the investigator for the study. If you withdraw your permission, you will not be able to stay in this study.

What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study.

You will be given a copy of this Research Participant HIPAA Authorization describing your confidentiality and privacy rights for this study.

By signing this document, you are permitting Penn Medicine to use and disclose personal health information collected about you for research purposes as described above.

Who can I call with questions, complaints or if I'm concerned about my rights as a research participant?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research participant, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the IRB at the number on page one of this form.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your protected health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that protected health information to outside organizations or people involved with the operations of this study.

A copy of this consent form will be given to you.

_____	_____	_____
Name of Participant **[print]**	Signature of Participant	Date
_____	_____	_____
Name of Person Obtaining Consent **[print]**	Signature	Date

We would like to be able to contact you in the future to see if you would be interested in participating in follow-up research studies. Please indicate below if we can store your identifiable information below so we can contact you for possible future research opportunities by checking the “yes” or “no” options.

____ Yes, I agree to have my identifiable information store for possible future contact.

____ No, I do not want to have my identifiable information store for possible future contact.

Participant Initials: _____ Date: _____