UNIVERSITY OF PENNSYLVANIA
RESEARCH SUBJECT
INFORMED CONSENT AND HIPAA AUTHORIZATION FORM

Protocol Title:	Promoting Recovery after Stroke with Amantadine (PRESTA)
Principal Investigator:	Scott Kasner, MD 3400 Spruce Street, Gates 3 Philadelphia, PA 19104 215-349-5990
Emergency Contact:	Scott Kasner 215-349-5990

RESEARCH STUDY SUMMARY FOR POTENTIAL SUBJECTS

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 assess whether amantadine, a drug commonly used to help patients with Parkinson's Disease, can help stroke patients recover.

If you agree to join the study, you will be asked to complete the following research procedures: neurological examination, cognitive testing, questionnaire about your recovery, and a test of your hand strength. You will be assigned at random (like flipping a coin) to receive either the study medication, amantadine, or placebo. Your participation in this study will last 90 days.

The possible side effects of amantadine may include orthostatic hypotension, feelings like you're about to faint, fainting, swelling in arms or legs, dizziness, delusions, hallucinations, falls, dry mouth, and constipation.

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.

WHO IS CONDUCTING THE RESEARCH STUDY?

This study is a local study being conducted and funded by the stroke division at the Hospital of the University of Pennsylvania, Pennsylvania Hospital, and Penn Presbyterian Medical Center.

The Principal Investigators of the study are Scott Kasner, MD and Aaron Rothstein, MD, both in the Department of Neurology at Penn Medicine.

WHY AM I BEING ASKED TO VOLUNTEER?

You are being invited to participate in a research study because you have had a stroke. A stroke is an injury to the brain caused by either a blocked or a ruptured blood vessel. Stroke is one of the leading causes of disability worldwide. And while we have therapies to help prevent further strokes and treat strokes while they are happening, there is very little we can do to help patients recover from strokes.

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?

This is a study enrolling patients with stroke to explore whether amantadine, a drug used often to help patients with Parkinson’s disease, can also be used to help patients recover from their stroke both physically and cognitively. Amantadine is approved by the U.S. Food and Drug Administration for treatment of Parkinson's disease but is not currently indicated for patients with stroke, and the use of this drug in this study is considered experimental.

HOW LONG WILL I BE IN THE STUDY? HOW MANY OTHER PEOPLE WILL BE IN THE STUDY?

Your participation will last for 90 days. You will be taking either amantadine or placebo for only 30 days. Your final round of tests will occur at 90 days. We expect that there will be a total of 60 patients in the study; 30 patients will be taking amantadine and 30 patients will be taking placebo.

WHAT IS INVOLVED IN THE RESEARCH STUDY?

If you are eligible for the study and you decide to participate, you will be "randomized" into one of the study groups described below. Randomization means that you are put into one of two groups completely by chance. It is like flipping a coin. You will receive

either placebo (inactive pill, which is the equivalent of not receiving any drug whatsoever) or amantadine.

Your study treatment will depend on which group you are assigned to:
Group 1: Amantadine 100 milligrams twice per day, or 100 mg once daily if 65 or older OR

Group 2: Placebo (inactive pill) twice per day (or once a day if 65 or older) that looks identical to the amantadine pill.

Neither you nor the researchers conducting this study will know or choose what group you will be in. You will have an equal chance of being placed in either group. However, in the event of an emergency, the researcher and your other physicians will be able to find out which treatment you are receiving.

STUDY PROCEDURES

Some of the study procedures are done only for research purposes. Your regular doctors will perform or provide the standard tests, and study doctors will oversee the study research procedures.

Research-Related Procedures:

- Neurological assessments measuring neurological function as well as cognitive abilities and mood
- Adverse Event review
- Review of medication adherence
- Review of any medications you take

Standard-Of-Care Procedures:

- Brain imaging: CT or MRI
- Pregnancy test, if applicable

Schedule of Study Visits

First Visit, Screening and Randomization: This visit will take about 30 minutes. This visit will occur as early as 1 day after your recent stroke and up to 21 days after. Activities at this visit include:

- Providing information about the study, answering your questions, and signing of this informed consent document;
- Reviewing your medical history information to make sure that all required standard tests have been performed and that you meet all the study criteria;
- Measuring how well you are functioning after your stroke;
- Performing a pregnancy test for sexually active women of child bearing potential
- Randomization and drug dispensing
- Scheduling the next visit, the follow-up visit.

Second Visit, Follow-Up: This visit may take up to 30 minutes. It will occur at 7 days after your First Visit. Activities at this visit include:
• Measuring how well you are functioning after your stroke;
• Assessing how well you are taking your medications and evaluating you for any side effects from study medication.

Additional Follow-Up Visits: These visits will occur at 30 days and 90 days after enrollment in the study and will take 20-30 minutes. Activities at these follow-up visits include:
• Assessing for any strokes or adverse events since you were last seen;
• Assessing how well you are taking your medications;
• Assessing what other medications you are taking;
• Collecting unused study medication; please bring the study medication bottles and any leftover study medication with you to each visit;
• Measuring how well you are functioning after your stroke.

In case you are not available for a follow-up visit, the study team may visit you at home or contact family members that you designate, so that you can be assessed for any strokes or serious adverse events since you were last seen.

Unscheduled visits may occur if the study doctor feels it is necessary to re-assess your health status.

The study staff may call you to remind you of an upcoming visit or contact you by mail, email, or text, if you agree to these reminders. After signing this consent, the study staff will ask you how you prefer to be contacted for reminders of study visits. Some of the procedures in this study are standard-of-care procedures that you should undergo even if you are not in the study.

We will notify your primary care doctor, if you have one, about your participation in this study prior to your enrollment (if possible) or early in your participation in the study, so they will understand that you are taking study medication. They can contact the study research team with any questions.

WHAT ARE THE POSSIBLE RISKS OR DISCOMFORTS?

There is no physical risk to taking part in the exams and filling out the questionnaires associated with this study. However, you may find them inconvenient because they take up your time.

As in any research study, it is possible that this study may involve risks that are currently unforeseeable.

AMANTADINE SIDE EFFECTS

If you are randomized to receive amantadine, there are risks of adverse reactions from the drug.

The most common side effects (in 5-10%) of patients taking this drug have been noted:

- Feeling dizzy or lightheaded
- Feeling like you're about to faint
- Nausea
- Insomnia
- Dizziness

Less frequently, in 1-5% of patients taking the drug, the following side effects have been noted:

- Depression
- Anxiety and irritability
- Hallucinations
- Confusion
- Anorexia
- Dry mouth
- Constipation
- Unsteadiness
- Rash (livedo reticularis)
- Swelling in arms or legs
- Feeling dizzy or lightheaded when standing up (orthostatic hypotension)
- Headache
- Somnolence
- Nervousness
- Diarrhea
- Dry nose
- Fatigue

Rare and infrequent side effects in <1% of patients include:

- Seizures
- Low white blood cell count (neutropenia)
- Suicidal ideation (SI)
- Congestive Heart Failure
- Urinary retention
- Visual disturbance

There have been some reports of muscle stiffness, fever and altered mental status (Neuroleptic Malignant Syndrome) after abruptly stopping the medication, particularly in patients taking antipsychotic medications, though this is not common.

In order to prevent some of these side effects, patients taking the drug are counseled to avoid getting up suddenly from a sitting or lying position and to avoid excessive alcohol

intake. Less common side effects are also possible, including impulse control disorders and melanoma although these have not been proven in the scientific literature to be a side effect of the medication.. If you have any potential side effects from the medication, call 215-349-5990

Call your doctor or get medical help right away and notify the PI if you have any of these signs or symptoms when taking study medications or immediately after stopping the study medication:

- Seizures
- Suicidal thoughts
- Blurred vision
- Fainting
- Psychosis (seeing or hearing people or voices that aren't there)
- Depression
- Muscle stiffness, fever, and altered mental status

REPRODUCTIVE RISKS

Because of possible amantadine side effects, there could be serious harm to unborn children or children who are breast-feeding. These effects could also harm the mother. It is also possible that harmful side effects that are not yet known could happen to both the mother and unborn or breast-feeding child. If you are currently pregnant, it is important that you inform the investigator because you will not be able participate in the study. If you are able to become pregnant, you will be given a serum pregnancy test before entry into the study. You are asked to use a medically accepted method of birth control while you participate in the study (condom use—male or female—with spermicide during sexual intercourse, an intrauterine device (IUD) or stable hormonal-based contraception). You should not become pregnant while you are taking this drug. If you do become pregnant, you must tell the investigator and consult an obstetrician or maternal-fetal specialist. We will continue to see you for your study visits and exams but will immediately stop your study medication.

GUIDANCE ON DISCONTINUING STUDY MEDICATION

There are times when you may need to stop your study medication, either for a short period or permanently. You must call the study staff who can work with your regular doctors to make the best and safest plan to stop the medication. Do not stop taking the medication unless your doctor tells you to. Your treating doctors can call the study staff and rapidly find out which study medication you are taking.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

You may choose either to take part or not to take part in this research study. If you decide not to participate, you will not lose any benefits to which you would otherwise be entitled. If you decide to take part, you may decide to leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to you.

You will be told of any important new information that is learned during the course of this research study which might affect your health, welfare, or willingness to continue participation in this study.

Nothing in this consent form waives any legal rights you may have nor does this consent form release the investigator, the University of Pennsylvania (institution), or its agents from liability for negligence. University of Pennsylvania employees and their family members do not have to be in this study. No one should influence or pressure you to be in this study. An employee's or his/her family member's decision to be in the study, or to leave the study early, will not affect the employee's job or job benefits

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?

If you agree to take part in this research study, you may not benefit directly even if you are randomized to amantadine. We hope the information learned from this research study will benefit other patients with stroke in the future.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT PARTICIPATE?
The alternative to participating in this research trial would be to receive standard-of-care medical treatment, which would typically mean rehabilitation with physical, occupational, and speech therapies.

WILL I BE PAID TO PARTICIPATE IN THIS RESEARCH STUDY?
No, you will not be paid to participate in this research study.

WILL I HAVE TO PAY FOR ANYTHING?
There are no extra costs for you to participate in this study.

Physical exams and all study visits performed as part of the study will not cost you anything. The study will pay for your study medications.

The study will not pay for the standard medical care that you receive during the course of the study. You are still responsible for any deductibles or applicable co-pays for routine 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 header.

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 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 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. Withdrawal will not interfere with your future care.

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. Except as required by law, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier outside of this trial. Your research records may be disclosed outside of The Hospital of the University of Pennsylvania, but in this case, your identifying information will be deleted, and you will be identified by a unique code number. This information will be kept in a secure location and access will be limited to research study personnel. The results of this research study may be presented at scientific or medical meetings or published in scientific journals. However, your identity will not be disclosed.

The Institutional Review Board (IRB) at the University of Pennsylvania will have access to your records, and patient information may be provided to federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction. At the end of the study, the information collected about you during the study will be

stripped of anything that could personally identify you, and then this anonymous information will be stored for use by other researchers in the future.

Your participation in this research study may be included in your electronic health record. Individuals providing service or care to you may be able to see it.

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. ClinicalTrials.gov is a database of publicly and privately supported clinical studies of human participants conducted around the world.

WHAT MAY HAPPEN TO MY INFORMATION COLLECTED ON THIS STUDY?
A federal regulation known as the Privacy Rule gives you certain rights concerning the privacy of your health information. Researchers covered by this regulation are required to get your authorization (permission) to use and disclose (share with others) any health information that could identify you. You should have received a Notice of Privacy Practices when you received health care services here. If not, let us know and a copy will be given to you.

If you sign this informed consent form, you are giving permission for the use and disclosure of your health information for purposes of this research study. You do not have to give this permission. Your health care outside of the study, payment for your health care, and your health care benefits will not be affected if you choose not to sign this form. However, if you do not sign this form, you will not be able to participate in the study.

FUTURE USE OF DATA AND/OR SPECIMENS
Your information will be de-identified. De-identified means that all identifiers have been removed. The information could be stored and shared for future research in this de-identified fashion. The information be shared with other researchers within Penn, or other research institutions, as well as pharmaceutical, device, or biotechnology companies. It would not be possible for future researchers to identify you as we would not share any identifiable information about you with future researchers. 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.

ELECTONIC 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 SUBJECT, 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.

We will delay sharing with you whether you were taking a placebo pill or amantadine until the end of the study. Test results and research visit notes will be shared with you as they are completed and entered into the medical record.

WILL I RECEIVE THE RESULTS OF RESEARCH TESTING THAT MAY BE RELEVANT TO MY HEALTH?

Results that may be relevant to your healthcare may be released to you. Clinically relevant results relating to your mood and cognition may change clinical management. As such, if there is concern, you will be provided with the appropriate clinical care. These results will be released in the EMR as soon as they are completed

WHAT INFORMATION ABOUT ME MAY BE COLLECTED, USED, OR SHARED WITH OTHERS?

The following personal health information (PHI) will be collected, used for research and may be disclosed during your involvement with this research study

- Name, address, telephone number, date of birth
- Electronic mail address
- Ethnic origin/race and gender
- Medical record Number
- Personal and family medical history
- Current and past diseases
- Current and past medications or therapies
- Information from a physical examination that generally also includes blood pressure reading, heart rate, breathing rate and temperature
- Results of tests and procedures you will undergo during this research study as described in this informed consent form

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?

Oversight organizations
• The Office for Human Research Protections and agencies (including the FDA) in the U.S. Department of Health and Human Services.
• A Data and Safety Monitoring Board and others authorized to monitor the conduct of the Study.

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 Subject Informed Consent and HIPAA Authorization Form 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 SUBJECT?

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 subject, 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 personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that personal 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 Subject (Please Print)	Signature of Subject	Date
_____	_____	
Name of Person Obtaining Consent (Please Print)	Signature	Date

For subjects unable to give authorization, the authorization is given by the following authorized subject representative:

_____	_____	
Authorized subject representative **[print]**	Authorized subject representative Signature	Date

Provide a brief description of above person authority to serve as the subject's authorized representative.

_____