MAYO CLINIC

Name and Clinic Number

Approval Date: **September 6, 2024**
Not to be used after: **July 31, 2025**

RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: A Multidisciplinary Translational Approach to Investigate the Mechanisms, Predictors, and Prevention of Persistent Post-Traumatic Headache **(Clinical Trial all sites)**

IRB#: 19-003200

Principal Investigator: Dr. Todd Schwedt and Colleagues

Key Study Information

This section provides a brief summary of the study. It is important for you to understand why the research is being done and what it will involve before you decide. **Please take the time to read the entire consent form carefully and talk to a member of the research team before making your decision.** You should not sign this form if you have any questions that have not been answered.	
It's Your Choice	This is a research study. Being in this research study is your choice; you do not have to participate. If you decide to join, you can still stop at any time. You should only participate if you want to do so. You will not lose any services, benefits or rights you would normally have if you choose not to take part.
Research Purpose	You are being asked to participate in this study because you have been diagnosed with post-traumatic headache (PTH) due to a mild traumatic brain injury (mTBI) or concussion. The purpose of this research study is to help find the cause of PTH and to determine why PTH goes away relatively quickly in some people but persists in others. In addition, this research will investigate a treatment for PTH, with the goal of preventing PTH persistence. There are currently no approved treatments for PTH. This research will investigate the safety and efficacy a drug called "erenumab" for the treatment of PTH.
What's Involved	Study participation involves up to 5 study visits at Mayo Clinic. You will receive monthly subcutaneous injection (under your skin) of erenumab 140 mg

	You will receive study treatment at the following post-enrollment time points: 4 weeks, 8 weeks, and 12 weeks (a total of 3 treatments).
Key Information	According to the FDA label for erenumab as a migraine treatment, contraindications to its use are "none." The risk section below further details the associated risks with the study drug. There will be no cost to you associated with tests performed solely for this research study. You may or may not benefit from being in this study. If you take part in this study, other people with PTH may benefit from what we learn in this research study. You don't have to be in this study to receive treatment for your condition. Other management approaches for your condition are available. If you have questions about these other management approaches, you should speak with your health care provider about the risks and benefits of these other choices.
Learn More	If you are interested in learning more about this study, read the rest of this form carefully. The information in this form will help you decide if you want to participate in this research or not. A member of our research team will talk with you about taking part in this study before you sign this form. If you have questions at any time, please ask us.

Making Your Decision

Taking part in research is your decision. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision. Taking part in this study is completely voluntary and you do not have to participate.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you either a printed or electronic copy of this form to keep.

For purposes of this form, Mayo Clinic refers to Mayo Clinic in Arizona, Florida and Rochester, Minnesota; Mayo Clinic Health System; and all owned and affiliated clinics, hospitals, and entities.

Contact Information

If you have questions about …	You can contact …
▪ Study tests and procedures ▪ Materials you receive ▪ Research-related appointments ▪ Research-related concern or complaint ▪ Research-related injuries or emergencies ▪ Withdrawing from the research study	**Principal Investigators:** Todd Schwedt, M.D. **Phone:** (480) 301-6574 (Arizona) Dmitry Esterov, D.O. **Phone:** (507) 285-3115 (Rochester) Kevin Barrett, M.D. **Phone:** (904) 953 -7102 (Florida) **Institution Name and Address:** Mayo Clinic Hospital 5777 East Mayo Boulevard Phoenix, AZ 85054 Mayo Clinic Rochester 200 First Street SW Rochester, MN 55905 Mayo Clinic Florida 4500 San Pablo Road Jacksonville, FL 32224
▪ Rights of a research participant	**Mayo Clinic Institutional Review Board (IRB)** **Phone:** (507) 266-4000 **Toll-Free:** (866) 273-4681
▪ Rights of a research participant ▪ Any research-related concern or complaint ▪ Use of your Protected Health Information ▪ Stopping your authorization to use your Protected Health Information ▪ Withdrawing from the research study	**Research Participant Advocate (RPA)** **(The RPA is independent of the Study Team)** **Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** researchparticipantadvocate@mayo.edu
▪ Billing or insurance related to this research study	**Patient Account Services** **Toll-Free:** (844) 217-9591

Other Information:
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.

A description of this research study will be available on www.MayoClinic.org. This Web site will not include information that can identify you. You can search this Web site at any time.

Why are you being asked to take part in this research study?

You are being asked to participate in this study because you have been diagnosed with post-traumatic headache (PTH) due to a mild traumatic brain injury (mTBI) or concussion. Based on your participation and the information you have provided thus far during the first post-traumatic headache study, you qualify to participate in the clinical trial portion.

Why is this research study being done?

The purpose of this research study is to help find the cause of PTH and to determine why PTH goes away relatively quickly in some people but persists in others. In addition, this research will investigate a treatment for PTH with the goal of preventing PTH persistence.

There are currently no approved treatments for post-traumatic headache. This research will study the safety and efficacy of a drug called “erenumab” for the treatment of PTH. In children, adults, athletes, civilian, and military populations, PTH closely resembles migraine. Erenumab is approved by the United States Food and Drug Administration for the treatment of migraine and might also be effective for treating PTH.

Information you should know

Who is Funding the Study?
The United States Department of Defense is funding the study. The Department of Defense will pay Mayo Clinic to cover costs related to running the study.

Study drug will be provided by Amgen, Inc. the manufacturer of erenumab.

Information Regarding Conflict of Interest:
Your healthcare provider may be referring you to this research study. If your healthcare provider is also an investigator on this study, there is the chance that his or her responsibilities for the study could influence his or her recommendation for your participation.

If you prefer, your healthcare provider will be happy to refer you to another investigator on the research study team for you to decide if you want to participate in the study and to see you for the research study activities while you are in the study.

How long will you be in this research study?

You will be in this study for up to 24 weeks, from the beginning of the run-in phase to the final study visit.

What will happen to you while you are in this research study?

Before any study-related tests and procedures are performed, you will be asked to read and sign this consent document. The study staff will review your medical history to see if you can be part of this study.

Based on your participation and the information you provided thus far during the first post-traumatic headache study, you qualify to participate in the clinical trial portion.

Visit 1:

- We will collect your vital signs.
- You will be asked to complete a urine pregnancy test (if you are a woman of childbearing potential).
  You will receive your first erenumab to treatment at this visit.

Electronic Daily Headache Diary:
Consistent with the requirements of your participation in the first post-traumatic headache study, you will be asked to complete a daily electronic headache diary for the next 12 weeks. You might be asked to complete the diary for an additional 4 weeks, during the 6th month following into the clinical trial.
The study staff will instruct you on how to access the electronic headache diary. On a daily basis, you will provide information about headaches that you might have had that day. Completing the headache diary will take a few minutes each day.

Treatment with Erenumab:
You will receive monthly subcutaneous injection (under your skin) of either erenumab 140 mg. You will receive treatment at study at the following post-enrollment time points: 4 weeks, 8 weeks, and 12 weeks (a total of 3 treatments).

When you receive the study treatment, a needle will be used to inject the medicine under your skin, causing a small hole or puncture. Injections will be administered in the abdomen (except for a two inch area right around the navel), thigh, or outer area of upper arm (if someone else is injecting you) according to your preference and will consist of two consecutive 70 mg injections. The second injection will not be given in the exact same spot as the first injection.

Visit 2 (4 Weeks):

- We will collect your vital signs.
- Review your electronic headache diary entries.
- Review any adverse events (side effects)
- You will be asked to complete a urine pregnancy test (if you are a woman of childbearing potential).
- You will be asked to complete questionnaires and assessments.
- You will receive your second dosage of erenumab or placebo as outlined in the section above.
- You will be asked to continue to complete the daily headache diary.

Visit 3 (8 Weeks):

- We will collect your vital signs.
- Review your electronic headache diary entries.
- Review any adverse events (side effects)
- You will be asked to complete a urine pregnancy test (if you are a woman of childbearing potential).
- You will be asked to complete questionnaires and assessments.
- You will receive your third treatment of either erenumab or placebo at this visit.
- You will be asked to continue to complete the daily headache diary.

Visit 4 (12 weeks):

- We will collect your vital signs.
- Review any adverse events (side effects)
- Review your electronic headache diary entries.

You will be asked to complete the headache diary during weeks 25 through 28.

Visit 5 (24) weeks:

- We will collect your vital signs.
- Review any adverse events (side effects)

- Review your electronic headache diary entries.

Future Contact Consent:
I give the researchers at Mayo Clinic permission to contact me for future research opportunities that may or may not be related to this study.

☐ Yes ☐ No Please initial here: _____Date: _____

FITBIR:
Data from this study may be submitted to the Federal Interagency Traumatic Brain Injury (FITBIR) informatics system. FITBIR is a computer system run by the National Institutes of Health that allows researchers studying traumatic brain injury to collect and share information with each other. With an easier way to share, researchers hope to learn new and important things about traumatic brain injury more quickly than before.

During and after the study, the researchers will send information about your health and behavior and in some cases, your genetic information, to FITBIR. However, before they send it to FITBIR, they will remove information such as name, date of birth, and city of birth, and replace that information with a code number. Other researchers nationwide can then file an application to obtain access to your study data for research purposes. Experts who know how to protect health and science information will look at every request carefully to minimize risks to your privacy.

You may not benefit directly from allowing your information to be shared with FITBIR. In the future, the information provided to FITBIR might help researchers around the world treat individuals with traumatic brain injury so that they have better outcomes. FITBIR will report on its website about the different studies that researchers are conducting using FITBIR data; however, FITBIR will not be able to contact you individually about specific studies.

You may decide now or later that you do not want to share your information using FITBIR. If so, contact the researchers who conducted this study, and they will tell FITBIR, which can stop sharing the research information. However, FITBIR cannot take back information that was shared before you changed your mind. If you would like more information about FITBIR, this is available on-line at http://fitbir.nih.gov.

I permit my data to be shared with the Federal Interagency Traumatic Brain Injury (FITBIR) informatics system.

☐ Yes ☐ No Please initial here: _____Date: _____

Tests done only for research purposes are not meant to provide clinical information or help care for you. The results are only important for research. Therefore, the results of tests done with your information will not be provided to you.

In the rare event that a finding might affect the health of you or your family, we will contact you and you can choose whether to receive or refuse the information. If you decide to follow up and further medical testing or care is needed, the costs will be billed to you or your insurance.

What are the possible risks or discomforts from being in this research study?

Possible Risks Associated with Erenumab:
Safety and contraindications to treatment with erenumab in people with PTH has yet to be established.

When used to treat migraine, erenumab has been shown to be well tolerated and associated with few side effects. The most common side effects are injection site reaction, constipation, muscle spasm and pruritus (itching). With the exception of injection site reaction (5.2%) these side effects were reported by less than 5% of patients in the research studies of erenumab for migraine. Constipation, sometimes with serious complications, was reported by approximately 3% of individuals receiving erenumab.

Development of hypertension and worsening of pre-existing hypertension have been reported following the use of erenumab in the postmarketing setting. Many of the patients had pre-existing hypertension or risk factors for hypertension. There were cases requiring pharmacological treatment and, in some cases, hospitalization. Hypertension may occur at any time during treatment but was most frequently reported within seven days of dose administration. In the majority of the cases, the onset or worsening of hypertension was reported after the first dose.

It is also possible that some people could have an allergic reaction to erenumab. Some allergic reactions can be life threatening. These reactions may occur immediately after a dose or many days later. Allergic reactions can cause a rash or itching; trouble breathing or wheezing; a drop in blood pressure; swelling around the throat, mouth and eyes; a fast heart rate; fever; sweating; or chills.
If you experience any of these symptoms, you should call the Study Doctor right away at (480) 301-8000 or seek medical attention. If it is not possible to contact the Study Doctor immediately, please go to an emergency room as soon as possible.

Additional risks have been reported since erenumab was approved in May 2018 include mouth/lip sores and skin and tissue disorders under the skin such as hair loss and rash.

Potential risks associated with erenumab use during pregnancy and lactation are not established. Thus, pregnancy and lactation are exclusions to participating in this study.

Protection Against Risks:
Individuals who are known to be pregnant or lactating will be excluded from study participation. Pregnancy testing is mandated for women of childbearing potential. A reliable form of contraception (for women of childbearing potential) is required through 16 weeks after the last dose of erenumab. Acceptable methods of birth control include not having intercourse, hormonal birth control methods, intrauterine devices, surgical contraceptive methods, or two barrier methods (each partner must use a barrier method) with spermicide. A reliable form of contraception must be started prior to or at the time of starting the run-in phase. Not being of childbearing potential is defined as any woman who:

- Post-menopausal by history is defined as:
    - At least 55 years of age with cessation of menses for 12 or more months, OR
    - Younger than 55 years of age but no spontaneous menses for at least 2 years, OR
    - Younger than 55 years of age and spontaneous menses within the past 1 year, but currently amenorrheic (e.g., spontaneous or secondary to hysterectomy), AND with postmenopausal gonadotropin levels (luteinizing hormone and follicle-stimulating hormone levels at least 40 IU/L) or postmenopausal estradiol level (less than 5 ng/dL) or according to the definition of "postmenopausal range" for the laboratory involved.
        OR
    - Underwent bilateral oophorectomy OR
    - Underwent hysterectomy OR
    - Underwent bilateral salpingectomy

Measures that will be taken to protect your health information: All information collected from study participants will be locked in a secure location. Identifying information will be removed from the data forms and replaced by unidentifiable codes. Electronic databases/spreadsheets will be password protected and only accessible to those with access rights.

Are there reasons you might leave this research study early?

You may decide to stop at any time. You should tell the Principal Investigator if you decide to stop and you will be advised whether any additional tests may need to be done for your safety.

In addition, the Principal Investigator, the study sponsor (the Department of Defense), or Mayo Clinic may stop you from taking part in this study at any time:

- If it is in your best interest,
- If you don't follow the study procedures,
- If the study is stopped.

If you leave this research study early, or are withdrawn from the study, no more information about you will be collected; however, information already collected about you in the study may continue to be used.

We will tell you about any new information that may affect your willingness to stay in the research study.

What if you are injured from your participation in this research study?

Where to get help:
If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator at your site listed in the Contact Information at the beginning of this form. Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research related injuries?
Care for such research-related injuries will be billed in the ordinary manner, to you or your insurance. You will be responsible for all treatment costs not covered by your insurance, including deductibles, co-payments and coinsurance.

What are the possible benefits from being in this research study?

You may or may not benefit from being in this study. While our study is research and is not guaranteed to offer you help, you may benefit from the treatment if it works. If you take part in this study, other people with post-traumatic headache may benefit from what we learn in this research study.

What alternative do you have if you choose not to participate in this research study?

You don’t have to be in this study to receive treatment for your condition. Other treatments for your condition are available. If you have questions about these other treatments, you should speak with your health care provider about the risks and benefits of these other choices.

What tests or procedures will you need to pay for if you take part in this research study?

You won't need to pay for tests and procedures which are done just for this research study. These tests and procedures are:

- Urine pregnancy test (for women of childbearing potential)
- Study drug erenumab or placebo
- Electronic headache diary

However, you and/or your insurance will need to pay for all other tests and procedures that you would have as part of your clinical care, including co-payments and deductibles.

If you have billing or insurance questions call Patient Account Services at the telephone number provided in the Contact Information section of this form.

Will you be paid for taking part in this research study?

You will be paid $50 for each completed research study visit (as outlined in the first consent form you signed).

You will also be paid $35 per month for completing your headache diary at least 80% of the time, for a total of up to $175 (as outlined in the first consent form you signed).

Payment for participation in research is considered taxable income and reportable to the Internal Revenue Service (IRS). Accounts Payable at Mayo Clinic will be given your name, address and Social Security number in order to issue a check for your study participation. If you receive research payments totaling $600 or more in a calendar year, a tax Form 1099 will be sent to you. For Mayo Clinic employees, research payments are included in your paycheck with applicable taxes withheld and reported on your Form W2 after calendar year-end.

Will your information or samples be used for future research?

Identifiable information such as your name, Mayo Clinic number, or date of birth may be removed from your information in this study, allowing the information to be used for future research or shared with other researchers without your additional informed consent.

How will your privacy and the confidentiality of your records be protected?

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study.

Research materials will be stored securely. Data stored on a computer will be password-protected and secure. Every effort will be made to keep medical information confidential.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use and share your health information for research and why they may need to do so.
Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission (or "authorization") to Mayo Clinic.

Your health information may be collected about you from:

- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.

Your health information will be used and/or given to others to:

- To do the research.
- To report the results.
- To see if the research was conducted following the approved study plan, and applicable rules and regulations.

Your health information may be used and shared with:

- Mayo Clinic research staff involved in this study.
- United States Department of Defense (DOD)

- Arizona State University (ASU) research staff
- Amgen
- Phoenix Veterans Affairs (VA)
- Translational Genomics Research Institute (TGen)
- University of Arizona
- Georgia Institute of Technology
- Researchers at other institutions who are approved by the Principal Investigator of this study
- The Mayo Clinic Institutional Review Board that oversees the research.
- Other Mayo Clinic physicians involved in your clinical care.
- Researchers involved in this study at other institutions.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.
- The sponsor(s) of this study and the people or groups it hires to help perform this research.
- A group that oversees the data (study information) and safety of this research.

How your information may be shared with others:

While taking part in this study, you will be assigned a code that is unique to you, but does not include information that directly identifies you.
This code will be used if your study information is sent outside of Mayo Clinic. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form.

If the results of this study are made public (for example, through scientific meetings, reports or media) information that identifies you will not be used.

In addition, individuals involved in study oversight and not employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

Is your health information protected after it has been shared with others?

Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private and it may no longer be protected by the Privacy Rule.

Your Rights and Permissions

Participation in this study is completely voluntary. You have the right not to participate at all. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to sign this form, but if you do not, you cannot take part in this research study.

Deciding not to participate or choosing to leave the study will not result in any penalty. Saying 'no' will not harm your relationship with your own doctors or with Mayo Clinic.

If you cancel your permission for Mayo Clinic to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

You can cancel your permission for Mayo Clinic to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
201 Building 4-60
200 1st Street SW
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Participant Advocate at:researchparticipantadvocate@mayo.edu.
Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission for Mayo Clinic to use and share your health information lasts until the end of this study, unless you cancel it. The study does not end until all data has been collected, checked (or audited), analyzed, and reported. Because research is an ongoing process, we cannot give you an exact date when the study will end. Sometimes this can be years after your study visits and/or activities have ended.

MAYO CLINIC

Name and Clinic Number

Approval Date: **September 6, 2024**
Not to be used after: **July 31, 2025**

Enrollment and Permission Signatures

Your signature documents your permission to take part in this research.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature

Person Obtaining Consent

- I have explained the research study to the participant.
- I have answered all questions about this research study to the best of my ability.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature