Subject Name: _____ Date: _____

Title of Study: Topiramate Treatment of Alcohol Use Disorders in African Americans_____

Principal Investigator Name: David Oslin, MD_____

Version date and version number: V9 3/8/21

Principal Investigator's Name: DAVID OSLIN, M.D.
Complete VA Address: CORPORAL MICHAEL J. CRESCENZ VA MEDICAL CENTER
38TH AND WOODLAND AVENUES
MAILSTOP 116, MIRECC
PHILADELPHIA, PA 19104

Name of Study Sponsor: Department of Veteran Affairs

WHY AM I BEING ASKED TO VOLUNTEER?

You are being asked to voluntarily participate in a research study because you drink alcohol on a regular basis and expressed an interest in trying to reduce or stop your drinking. Your participation is voluntary, which means you can choose whether or not you want to take part. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. The study doctor will talk to you about the research study, and they will give you this consent form to read. You are encouraged to discuss this study and consent form with your family, friends, or family doctor. You may find some of the medical language difficult to understand. Please ask the study doctor about the study. If you decide to participate, you will be asked to sign this form and you will receive a signed copy.

WHAT IS THE PURPOSE OF THIS RESEARCH STUDY?

The purpose of this research study is to evaluate the safety and effectiveness of topiramate in reducing alcohol use among African-Americans who want to stop or reduce their drinking. This is a research study involving a medication (topiramate or a placebo (a harmless, inactive substance)), plus brief counseling to help reduce or stop drinking. Topiramate is approved by the U.S. Food and Drug Administration to treat epilepsy, prevent migraine headaches and, combined with another medication (phentermine), for weight loss. Its use in the treatment of alcohol use disorder is experimental. An earlier study by this research team showed that topiramate was more effective than placebo among European-Americans and it is important to find out if the medication has the same effect among African-Americans.

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

You will be involved with this study for approximately 9 months. You will have 13 study visits. The visits include one screening visit, 10 treatment visits over 13 weeks and two follow-up visits (at 3 and 6 months after the treatment ends). The study is also taking place at the Atlanta VAMC. We plan to enroll up to 100 Veterans from the CMCVAMC and Atlanta VAMC.

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WHAT AM I BEING ASKED TO DO?

While participating in this study you will receive either topiramate (the active drug) or placebo (an inactive substance). Twice as many people will receive the active topiramate versus getting placebo. Whether you receive either topiramate or placebo in the study will be assigned randomly like the flip of a coin. You and the study staff will not know if you are receiving the active drug, but this information is available 24 hours a day in case of medical need. The maximum study dose of topiramate is 200mg. The doses planned for this study are within the recommended guidelines for use of the medication in other conditions. Before starting the medication, you will meet with the study doctor to answer any questions you have. Study medication will be provided in capsules and will be packaged in child-resistant bottles. It is important that you follow the instructions on when and how to take the study medication.

You will also receive brief counseling. A study clinician will discuss ways to help you reduce or stop your drinking. With your permission, we will make an audio recording of each in-person counseling session. These recordings will be destroyed after they have been reviewed.

At the screening visit, you will be given the opportunity to read this consent form and ask questions. If you were mailed this form, we will ask you to return it in the provided pre-paid envelope. We will wait until we receive the signed form to complete the rest of the visit. After the screening is complete, we will determine if the study is a good match for you.

The chart below includes details about each visit. Parts of the visits may be completed by phone or video and other parts must be in-person at the CMCVAMC. We will ask you to complete at least 3 in-person visits during the study to measure your weight, blood pressure and pulse, and to draw blood. You will need to have an in-person visit before receiving study medication.

Visit Number	Visit Purpose and main components	Time
Screening Visit	Screening – to determine is study is a good fit for you • Questions about when you last drank alcohol • Consent • Standardized questionnaires • Medical history and physical exam - *in-person* • Blood draw for clinical labs and DNA (3 tablespoons of blood, DNA optional) - *in-person* • Urine sample for drug test and pregnancy if female- *in-person*	2 ½ hours

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Visit 1	Assign study medication • Weight, blood pressure, heart rate at in person visits • Brief counseling (30 min) • Receive study medication, review dosing instructions • Standardized questionnaires	1 ½ hours
Visits 2-9 (*visits are weekly from visits 1-6, then every other week for 7-9*)	Treatment Visits • Brief counseling (15 min) • Receive study medication (the dose will be increased each week during weeks 2-6 and tapered at visit 9) – *may be sent by mail* • Discuss any side effects you've experienced • Return study medication bottles and any remaining capsules- *may be returned by mail with per-paid postage* • Standardized questionnaires • Weight, blood pressure, heart rate at in-person visits • Visit 6 only: blood draw (1 tablespoon of blood) – *in-person* • Visits 5, 6, 7 and 9, females only: urine pregnancy test – *test may be sent by mail for home use*	30-45 minutes
Visit 10	Last Treatment visit • Brief counseling (15 min) • Return study medication bottles and any remaining capsules - *may be returned by mail with per-paid postage* • Discuss any side effects • Weight, blood pressure, heart rate - *in-person* • Blood draw (1 tablespoon) - *in-person* • Standardized questionnaires • Discuss setting up further treatment at the VA, which can include topiramate	1 hours
Visits 11 & 12	Months 3 and 6 Follow-up visits • Standardized questionnaires • Weight, blood pressure, heart rate - *in-person* • Blood draw (1 tablespoon) - *in-person*	1 hour

If you choose to withdraw from the study early, we will conduct safety evaluations and discuss follow-up care as well as for the study staff to instruct you on how to decrease and stop taking the study medication.

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Will I be paid for being in this study

You will be paid for your time and effort for completing different parts of the study. The total amount is up to **$450,** depending on the parts of the study that you complete:

Amount	**Specific part of the study**
$50 (x5)	Screening visit, Visits 1, 10, 11 and 12
$5 ($40 if you return all bottles)	Returning study medication bottles at visits 2-9
$20 (x8)	Visits 2-9

*If you complete some but not all of visits, you will receive a partial payment based on how much of the visit you complete.

Payments will be given in the form of vouchers. You can bring the voucher to the VA agent cashier to redeem for compensation or study staff can submit the voucher for direct deposit into your bank account. Vouchers can be redeemed for six months from the date on the voucher.

WHAT ARE THE POSSIBLE RISKS OR DISCOMFORTS?

Risks and side effects associated with topiramate.

Adverse effects of topiramate occurring more often than placebo and in more than 5% of subjects):

Numbness/Tingling	51	Difficulty with memory	7
Fatigue	15	Insomnia	7
Loss of appetite	15	Language problems	6
Upper respiratory tract infection	14	Abdominal pain	6
Nausea	13	Difficulty with concentration/attention	6
Diarrhea	11	Mood problems	6
Dizziness	9	Sinusitis	6
Weight loss	9	Sore throat	6
Changes in taste	8	Upset stomach	5
Reduces touch sense	7	Anxiety	5
Excess sleep	7		

Sudden worsening of vision and an elevation of fluid pressure in the eyes has been described in a few cases (less than 1%) of patients taking topiramate, usually at the beginning of treatment. If you have a sudden, significant worsening of vision, blurred vision, or eye pain you should contact study staff immediately, or if that is not possible, you should seek emergency care.

A severe increase in the level of acidity in the blood may result from topiramate treatment. This effect was experienced by about 3 to 7% of participants in other studies of topiramate. This can cause symptoms such as tiredness and loss of appetite, or more serious conditions including irregular heartbeat or coma. If this condition lasts, it can result in thinning of the bones and an increased risk for fractures as well as kidney stones.

Kidney stones are less likely to occur with topiramate treatment but are potentially serious (experienced by about 1.5% of participants). Drinking an adequate amount of fluids is recommended while taking topiramate. This may reduce the risk of kidney stones.

Overdoses of topiramate have been associated with convulsions, drowsiness, speech disturbance, blurred vision, double vision, impaired mental activity, abnormal coordination, stupor, hypotension, abdominal pain, agitation, dizziness and depression. Deaths have been reported in overdoses. You should take the medication only as prescribed for you.

Topiramate may cause a change (increase or decrease) in the effect of some other medications. If you are taking other medications during your participation in this study, your doctor will explain whether topiramate may have an effect and if necessary, may adjust your study drug dose.

Due to the possibility of dizziness or drowsiness, you must be cautious when operating a vehicle or heavy equipment while taking topiramate.

What safeguards to take?
We will ask about any side effects or other adverse events that you may experience. If you experience any side effects, please contact our study staff immediately. You can call our 24-hour pager at (215) 505-3799 during non-office hours and enter your telephone number for him/her to call you back or call Dr. David Oslin at (215) 823-5894 during the day.

The study drug must be kept out of the reach of children**.** Please do not share your study drug with others as it may have unpredicted negative side effects in other individuals. You have been screened for safely taking the study drug, but others have not undergone this screening.

Risks associated with blood draws.
There will most likely be some mild discomfort from the blood draw. Some people develop a bruise at the needle site; some people report dizziness after the blood is drawn; and, some people develop minor infections. Other risks of blood drawing include possibly fainting.

Safeguards to be taken for blood draws.
Only study staff or VA staff phlebotomists trained to perform venipuncture will perform the blood draws. The puncture site will be wiped with a disinfectant before the needle is inserted. Only sterile needles will be used. The puncture site will be covered with a bandage. You will be seated at the time blood is drawn and may lie down if you feel faint.

Risks for women of childbearing potential and safeguards to be taken:
Topiramate is labeled by the Food and Drug Administration as a category D medication. This means that there are data in humans from investigational or marketing experience showing that topiramate can cause harm to the fetus. Data from pregnancy registries show that infants exposed to topiramate in utero have an increased risk for cleft lip and or cleft palate (oral clefts). Therefore, participation in this study could possibly have an adverse effect on a developing fetus. You must inform the study physician/study nurse if you are pregnant/possibly pregnant. As part of the screening process and before you take the first dose of study drug, a urine pregnancy test will be done if you are able to become pregnant or are less than two years post-menopausal. You will also have urine pregnancy tests at visits 1, 5, 7, and 9. If you have had a hysterectomy, then a pregnancy test will not be required. While you are participating in this study, you must continue to use an effective method of birth control.

Acceptable methods of birth control include: the birth control pill, intrauterine device, injection of Depo-Provera, Norplant, contraceptive patch, contraceptive ring, double-barrier methods (such as condoms and diaphragm/spermicide), male partner sterilization, abstinence (and agreement to continue abstinence or to use an acceptable method of contraception, as listed above, should sexual activity commence), and tubal ligation.

It is possible that topiramate may make some hormonal contraceptives (e.g., birth control pills, implants or injections) less effective. If necessary, your study doctor will discuss alternatives or non-hormonal methods of birth control with you to use during the study. If you are using hormonal contraceptives, you should report to the study nurse any change in your bleeding patterns.

If you become pregnant during this study, you must tell the study doctor and consult an obstetrician or maternal-fetal specialist. The study medication will be stopped immediately.

Risks associated with confidentiality and safeguards taken
Every attempt will be made by the investigators to maintain all information collected in this study strictly confidential. In addition to study staff, authorized representatives of the VA will have access to and may copy, both your medical records and records from your participation in this study. This access is necessary to ensure the accuracy of the findings and your safety and welfare. If any publication or presentations result from this research, you will not be identified by name. The data are kept in secure, locked areas and can only be accessed through the study team.

If we learn that you or someone else is in serious danger of harm (such as in cases of child or elder abuse) we may make disclosures to protect you and/or the other persons.

What other types of risk are involved if I choose to participate?
The study assessments will address potentially sensitive matters, including your drinking, drug use, psychiatric symptoms, and possible health, legal, family, and other problems. The counseling you receive will not differ much from standard medical counseling for drinking problems and should pose no particular risk to you. However, it is possible that the counseling, even when accompanied by topiramate, may not adequately help you to reduce your drinking to non-hazardous levels. Discussing sensitive issues may also make you feel uncomfortable.

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 may not benefit from participating in this research study. You may benefit from the screenings and medical examinations and brief therapy provided during the study. You may have a good response to the study medication and successfully reduce drinking. However, it is possible that you will receive no direct health benefit from being in this study. Other people who have alcohol problems may benefit from the information learned from the study in the future. We might find a better way to treat them. Societal benefits may include a better understanding within the medical community of how best to treat heavy drinking. However, there is also the possibility that no benefit will come from this study.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT PARTICIPATE?

You have the choice not to participate in this research study. Participation is voluntary and you do not have to participate if you do not want to. If you choose not to participate in the study, alternative options are available to you. You may obtain treatment with other medications (including three that are approved for the treatment of alcohol dependence: acamprosate, disulfiram and naltrexone), and standard counseling, including individual and group therapy. You could also request that your medical provider prescribe topiramate to treat your alcohol problem.

GENETIC RESEARCH

An optional component of the study is to give a blood sample that may be used to extract your DNA, which contains genetic information that you got from your parents. We plan to use your genotype (DNA) to test it with your response to the study medication. There is some evidence that people with certain genetic information respond better to topiramate and we want to test for this effect in this study.

Testing of your DNA will be done for research purposes only. Because the results have no clear meaning at this time, we will not report the genetic test results to you or your doctors and we will not add them to your medical record. All samples will be destroyed at the end of the study.

The main risk of genetic testing is breach of confidentiality, with sensitive information concerning your genetic risk for disease becoming known. Your DNA will be labeled with a study code instead of your name or other information that could identify you. The key that links the study code to your identity will be kept at the VA. Only a few authorized VA employees will have access to that key.

Federal laws and policies provide you with protection from discrimination by health insurance companies, group health plans, and most employers based on your genetic information. A new federal law, the Genetic Information Nondiscrimination Act (GINA) generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information obtained from this research.
- Health insurance companies and group health plans may not use your genetic information obtained from this research when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information obtained from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

The Veterans Health Administration has internal policies similar to GINA that do not allow the use of your genetic information to deny benefits to you under the Veterans Health Benefit Plan.

WILL I HAVE TO PAY FOR ANYTHING IF I PARTICIPATE IN THIS STUDY?

You will not have to pay for any research procedures or tests that result from participating in this study.

WHO CAN SEE OR USE MY INFORMATION? HOW WILL MY PERSONAL INFORMATION BE PROTECTED?

During the course of this study, we will collect personal information, including:

- Name
- Social Security/Medical Record Number
- Street and email addresses
- Dates of visits
- Progress notes from CPRS
- Laboratory and diagnostic values
- Alcohol and drug use and abuse history
- Current medications
- Audio recordings of treatment sessions

Your name and social security/medical record number will be used only as necessary within the CMCVAMC. But other private information may be disclosed to the study sponsor, the Department of Veteran Affairs. If you have an accident or reaction during the course of the study, your entire medical record may be used and disclosed as clinically necessary.

Internal monitors from the CMCVAMC Institutional Review Board (IRB), a research oversight committee, may inspect study records for quality assurance. This informed consent document will be added to your medical record. The results of this study may be published; however, you will not be identified by name or other personal identifiers. Further, your medical records will not be revealed unless required or authorized by law.

Once you are enrolled in the study, you will be given a unique study number. Only that number will be recorded on all study information. The code that links your name with your study number will always be kept locked. Paper study records will be kept locked in Dr. Oslin's research offices located in Building 1 of the CMCVAMC, 2nd Floor, Room B228. Electronic data will be stored on a password-protected server at the VA. Access to study records is limited to study staff.

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The University of Pennsylvania Investigational Drug Service (IDS) will supply the study medication for this study. The lab staff will be given your name, study identification number, and dates of your study visits. If they mail you medication, they will also be given your address and phone number.

DNA samples may be sent to the laboratory of Richard Crist, Ph.D. at the University of Pennsylvania Translational Research Lab for DNA analysis and then will be destroyed.

The required records, including the investigator's research records, must be retained until disposition instructions are approved by the National Archives and Records Administration and are published in the VHA's Records Control Schedule (RCS 10-1).

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.

SPECIAL CIRCUMSTANCES

You may need to be discontinued from study medication if you have serious or persistent complaints of adverse effects that are likely due to the study medication. You may also need to be discontinued from study medication if you have abnormal liver enzyme lab values confirmed with a repeat blood test, if you have any condition which Dr. Oslin finds the medication may be a hazard to you, or if you develop a medical illness or condition that requires hospitalization.

WHAT SHOULD I DO IF I HAVE BEEN INJURED OR EXPERIENCE A MEDICAL PROBLEM?

It is important that you tell your study doctor, Dr. Oslin, if you feel that you have been injured because of taking part in this study. You can call Dr. Oslin at **215-823-5894** during the day or call a study psychiatrist after hours at **(215) 505-3799** (this is a UPenn beeper and you will be prompted to enter your telephone number to receive a call back). If it is an emergency and assistance is not available by these methods, go to the nearest emergency room.

WHEN IS THE STUDY OVER? CAN I LEAVE THE STUDY BEFORE IT ENDS?

You understand that you do not have to take part in this study, and your refusal to participate will involve no penalty or loss of rights to which you are entitled. You may withdraw from this study at any time without penalty or loss of VA or other benefits to which you are entitled. If you withdraw, you may be asked to return for a final study visit in order to assure your safety. You should withdraw in writing using the Revocation of Authorization for Use & Release of Individually Identifiable Health Information for Veterans Health Administration Research form at the end of this informed consent document. Even if you withdraw, we can continue to use information about

you that has been collected up to that point. No information will be collected after you formally withdraw in writing.

If you wish to withdraw from the study, you must contact a member of the research staff. You will be asked to complete a final visit to conduct safety evaluations, return unused study medication, safely taper you off study medication and to discuss treatment options.

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 if 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.

WHAT ARE MY RIGHTS AS A RESEARCH SUBJECT?

You have read or have had read to you all of the above. Dr. Oslin or his designee has explained the study to you and answered all of your questions. You have been told of the risks or discomforts and possible benefits of the study. You have been told of other choices of treatment available to you.

In case there are medical problems, research related injuries or questions, you have been told that you can call Dr. Oslin at (215) 823-5894 or a study Psychiatrist after hours (215) 505-3799.

If you would like to discuss problems, complaints, concerns, or questions with someone who is not directly associated with your participation in this study or you have any questions regarding your rights as a research subject or you want to check the validity of the study and its personnel within the VA, you should contact the Research Compliance Officer at 215-823-7847 or the Patient Representative at 215-823-5803 from 8:00 AM to 4:30 PM Monday through Friday.

If you have concerns or complaints about the research study, you may contact the research staff involved with this study at (215) 823-5894.

As a Veteran, we value your input into how research is conducted at the CMCVAMC. If you would like to offer suggestions and opinions, or if you would like to participate in future discussions of research in Philadelphia, please call the Research and Development (R&D) Administrative Officer at (215) 823-6020 or R&D Associate Chief of Staff at (215) 823-5893.

Every reasonable safety measure will be used to protect your well-being. The CMCVAMC will provide necessary medical care and treatment for any injury that is a result of participation in this

study for Veterans. Compensation for such an injury may be permitted by applicable federal laws and/or regulations. The VA is not required to provide treatment for injuries in research studies if the injuries are caused by your non-compliance with study procedures.

There will be no cost to you for participation in this study. However, some Veterans are required to pay co-payments for medical care and services provided by the VA. These co- payment requirements will continue to apply to medical care and services provided by the VA that are not part of this study. If you decide to participate in this study, you cannot be charged nor your insurance billed for research-related interventions or procedures that are required by the protocol.

You voluntarily consent to participate in this study. You confirm that you have read this consent document, or it has been read to you and that it explains what this research project is about and how and why it is being done. You will receive a signed copy of this document upon your signature.

Audiotaping of counseling sessions:

_____ ☐ I agree to the audio recording of my in-person study counseling sessions.
initials

_____ ☐ I do NOT agree to the audio recording of my study counseling sessions.
initials

_____ _____
Subject's Signature (required) **Date (by Subject)**

_____
Print Subject's Name (required)

_____ _____
Signature of Person Obtaining Consent (required) **Date (by Person Obtaining Consent)**

_____
Print Person Obtaining Consent's Name (required)

APPROVED by CMCVAMC IRB on 04/21/2021

Terri Laufer, MD, IRB Chair