UNIVERSITY OF MINNESOTA

Title:	Role of Neurogenic Inflammation and Topical 6% Gabapentin Therapy in Symptomatic Scarring Alopecia
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Study Drug:	Gabapentin 6% Solution
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List of Abbreviations

CGRP	Calcitonin Gene-Related Peptide
CFR	Code of Federal Regulations
CRF	Case Report Form
CTCAE	Common Terminology Criteria for Adverse Events
DLQI	Dermatology Quality of Life Index
ELISA	Enzyme-linked Immunosorbent Assay
FDA	Food and Drug Administration
GABA	Gamma -Aminobutyric Acid
GCP	Good Clinical Practice
ICH	International Conference on Harmonization
IDS	Investigational Drug Services Pharmacy
IRB	Institutional Review Board
H&E	Hematoxylin and Eosin Stain
LPP	Lichen Planopilaris
LPPAI	Lichen Planopilaris Activity Index
PSA	Primary Scarring Alopecia
SF-36	Short Form (36) Health Survey
UPIRTSO	Unanticipated Problems Involving Risk to Subjects or Others
VAS	Visual Analog Scale

Study Summary

Title	Role of Neurogenic Inflammation and Topical 6% Gabapentin Therapy in Symptomatic Scarring Alopecia
Short Title	Scarring alopecia – Gabapentin study
Methodology	Cohort study
Study Duration	16 weeks for each subject
Study Center(s)	Single-center
Objectives	To determine the role of neurogenic inflammation in scarring alopecia and to assess the safety and efficacy of topical gabapentin in the management of symptomatic scarring alopecia.
Number of Subjects	10 (ten)
Diagnosis and Main Inclusion Criteria	Biopsy-proven scarring alopecia; Men and women greater than 18 years of age. Their scarring alopecia should be symptomatic with symptoms including burning, tingling, itch, pain in addition to hair loss. The subject should have no history of use of neuromodulatory agents two months prior to study enrollment.
Study Product, Dose, Route, Regimen	Gabapentin 6% solution The maximum daily dose of topical gabapentin will be 2 ml with the estimation that no more than one-third of a subject's scalp is affected. The drug will be administered topically by the subject to symptomatic areas of intact skin two times daily for 12 weeks. Based on its half-life of 8 hours when taken orally, gabapentin will be administered two times a day and the dose will not exceed the amount of topical agent used on average to treat the entire scalp in everyday clinical practice (1 mL twice daily, 60 mL per month).
Duration of administration	The drug will be topically applied by the subject two times daily for 12 weeks.
Reference therapy	This is a pilot study and there is no reference therapy against which topical 6% gabapentin will be compared.
Statistical Methodology	An intent-to-treat analysis will be performed in all subjects with symptoms comparing the last visit to baseline.

1 Introduction

This document is a protocol for a human research study. This study is to be conducted according to US and international standards of Good Clinical Practice (FDA Title 21 part 312 and International Conference on Harmonization guidelines), applicable government regulations and Institutional research policies and procedures.

1.1 Background

Primary scarring alopecias (PSAs) are poorly understood dermatologic disorders that result in permanent hair loss (1). PSAs are classified based on the type of inflammatory infiltrate recognized histologically on biopsy: lymphocytic, neutrophilic, or mixed. As painful hair loss disorders, scarring alopecias have yet to be studied in a manner that explores the disease burden on the individual and how to more effectively manage debilitating symptoms. Most of the scarring alopecias involve a painful course, with individuals reporting scalp pain, burning, itching, or tingling/crawling sensations that can ultimately impact physical and psychological health (1). It is well-documented that individuals with chronic pain are more susceptible to depression and other mood disorders (2). Thus, a better understanding of the pain process in scarring alopecia would benefit patients and health care providers tremendously as scientists research to discover the origin and pathogenesis of these inflammatory and irreversible conditions.

CGRP (calcitonin gene-related peptide) has been proposed to play a role in pain transmission and inflammation (3, 4). While originally found to be elevated in migraines, two patients with lichen planopilaris (LPP) at the University of Minnesota were found to have elevated amounts of CGRP via immunohistochemical staining and confocal microscopic examination of scalp biopsy specimens. Seven patients, three with frontal fibrosing alopecia and four with LPP, were also found to have decreased expression of epidermal nerves as well as CRGP expression. This suggests that neurogenic inflammation may contribute to the disease state of scarring alopecia. Investigating this relationship between CGRP and scalp symptoms such as pain in the setting of scarring alopecia may lead to a long awaited breakthrough in disease pathogenesis and management. Agents that reduce the release of neuropeptides, such as gabapentin, may serve as potential treatment in scarring alopecia. Recent data from pilot experiments at the University of Minnesota using normal human tissue stimulated by gabapentin reflected a reduction in CGRP compared to levels of CGRP in control unstimulated tissue, indicating that CGRP may realistically be an appropriate therapeutic target in scarring alopecia.

1.2 Investigational Agent

Gabapentin is a GABA analogue originally introduced in 1994 for the treatment of epilepsy by Warner-Lambert (today Pfizer). It is currently widely used to relieve pain, especially neuropathic pain syndromes associated with diabetic neuropathy, vulvodynia, postherpetic neuralgia and other allodynia (5, 6). While gabapentin's mechanism of action is not completely understood, it is thought to work through its effects on voltage-gated calcium ion channels in the central nervous system once it crosses the blood-brain barrier (7). Its neuromodulatory effects also impact the peripheral nervous system.

1.3 Preclinical Data

Currently, the management of symptomatic scarring alopecia includes intralesional triamcinolone injections alone or with topical steroid solutions, minoxidil, oral antibiotics, hydroxychloroquine or immunosuppressive medications such as prednisone. Since the cause of scarring alopecia is unknown, the various modes of treatment have focused on targeting the inflammation associated with the disease process that is reflected histologically. No one treatment has been found successful in all conditions nor is there a cure. Individuals with end-stage, non-symptomatic disease may be candidates for hair transplantation.

1.4 Clinical Data to Date

There has been no study of topical neurogenic agents, such as gabapentin, to treat scarring alopecia. However topical gabapentin has been safely used in other conditions associated with chronic pain, burning, irritation, itch, or tingling, such as vulvodynia (5).

Interestingly, gabapentin has been shown to be effective against migraine headaches, a condition associated with high levels of CGRP (6). Gabapentin has also been shown to be effective in managing neuropathic pain. This evidence suggests that gabapentin could be effective in the treatment of scarring alopecia, especially if increased CGRP is contributing to symptomatology.

This study will serve as a pilot study to determine the efficacy and safety of topical gabapentin in the treatment of symptomatic scarring alopecia. In this study, 10 subjects with symptomatic lymphocytic-type scarring alopecia will be recruited and treated with topical gabapentin. Disease burden will be evaluated before and after 12 weeks of treatment through reporting of subjective symptomatology via surveys/questionnaire, neurometer study, clinical assessment, and biopsies measuring levels of CGRP before and after treatment.

1.5 Dose Rationale and Risk/Benefits

The maximum daily dose of topical gabapentin will be 2 mL daily. The drug will be administered topically by the subject to symptomatic affected areas of intact skin two times daily for 12 weeks. Subjects will be seen in follow up on Week 8 and Week 12 (Visits 4 and 5).

Gabapentin will be compounded into a 6% solution based on a preparation method described by Boardman et al. (5) and approved by Investigational Drug Services (IDS) Pharmacy, University of Minnesota. IDS will prepare and dispense the drug.

From published data in which gabapentin was used in a cohort group with nerve-related symptoms from localized or generalized vulvodynia, the most frequently reported adverse effect was irritation at the site of application, which led to termination of use (8%). Common adverse effects of oral gabapentin, including dizziness, somnolence, and peripheral edema, were not reported by any of the patients studied with vulvodynia. In this pilot study for scarring alopecia, the maximum daily dose will not exceed 2 mL of topical gabapentin 6% solution to affected scalp surface.

Based on its half-life of 8 hours, gabapentin will be administered two times a day during waking hours and the dose will not exceed the amount of a topical agent used on average to treat the entire scalp in everyday clinical practice (60 ml per month).

Subjects may directly benefit from analysis of nerve function, CGRP neuropeptide, and treatment with gabapentin, resulting in improvement of their symtoms that may prevent further hair loss and even possible hair growth. This analysis will also help us better understand the disease process in scarring alopecia to further improve management of the condition.

2 Study Objectives

Primary Objective: To assess the role of neurogenic inflammation associated with CGRP expression in scarring alopecia

Secondary Objective: To assess the safety and efficacy of topical 6% gabapentin in subjects with symptomatic scarring alopecia.

3 Study Design

3.1 General Design

This is a cohort study.

Every subject is expected to schedule 6 visits total to complete the study. The total duration of the study for each volunteer is expected to be approximately 14 weeks.

Prior to gabapentin treatment, there is one visit to screen individuals for participation in the study and to obtain consent. After consent is signed, this visit will also include obtaining history from the subject, clinical evaluation, survey completion, neurometer study, photography, and scalp biopsies. At this initial visit, a total of four 4-mm skin biopsies will be collected. Two biopsies will be collected from affected, symptomatic scalp, and two skin biopsies will be collected from clinically unaffected scalp. Routine histology, confocal microscopy examination, and, if indicated, ELISA CGRP level analysis will be performed on the biopsy specimens. Subjects will start topical 6% gabapentin treatment on Visit 2 (Day 0). Four remaining visits will be scheduled to follow subjects after the start of topical 6% gabapentin treatment. Visits 3, 4 and 5 will occur 4, 8 and 12 weeks respectively after treatment with gabapentin is started. These visits will include labwork to check gabapentin blood levels. During Visit 5, the subject will also be reassessed through clinical evaluation, completion of surveys, neurometer study, photography, and four 4-mm scalp biopsies. Visit 6 will be a follow-up visit two weeks after completion of treatment for suture removal and clinical evaluation of the subject.

TABLE 1. Schedule of Study Procedures

Schedule of Study Procedures	**Visit 1** Screening/ Baseline	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6** Follow-up
	Day -14	Day 0	Week 4	Week 8	Week 12	Week 14
Approximate visit duration	2-4 hours	30 min	30 min	30 min	1-2 hours	20 min
Assess inclusion/exclusion criteria, obtain informed consent	X					
Obtain medical history						
Physical examination of scalp	X				X	
Review changes in medical history and medications						
Surveys[a]	X		X	X	X	
Neurometer study[b]	X				X	
Record adverse experiences			X	X	X	X
LPPAI clinical assessment[c]	X	X	X	X	X	
Gabapentin blood level			X	X	X	
Skin biopsies	X				X	
Biopsy suture removal		X				X
Photographs[d]	X				X	
Topical gabapentin 6% solution BID to affected area		X	X	X		

[a]Surveys include the Dermatology Life Quality Index (DLQI), Short Form (36) Health Survey (SF-36), Pain Visual Analog Scale (VAS) and Itch Visual Analog Scale (VAS).
[b]Neurometer study will be performed on three areas: the index finger; normal-appearing, unaffected scalp; affected symptomatic scalp.
[c]Lichen Planopilaris Activity Index (LPPAI) clinical assessment was developed by *Chiang et al.* and published in JAAD in January 2010[24].
[d]Photographs will focus on the affected symptomatic areas of the scalp at Visit 1. Photographs of the same areas will be taken at Visit 5.

3.2 Primary Study Endpoints

(1) To assess the role of neurogenic inflammation in symptomatic scarring alopecia and (2) assess the efficacy of topical 6% gabapentin in the management of symptomatic scarring alopecia patients. Subjects' disease burden will be assessed by clinical exam, qualitatively with surveys and neurometer study, and skin biopsies to confirm disease diagnosis, assess disease inflammation, and measure CGRP levels. Subjects will begin topical 6% gabapentin treatment for 12 weeks starting at Visit 2. They will be followed up every 4 weeks during treatment and will be reassessed at week 12 (visit 5) with clinical exam, qualitatively with surveys and neurometer study, and final biopsies to evaluate the impact of gabapentin on the disease and CGRP levels. The surveys to be filled out by the subjects include the Dermatology Life Quality Index (DLQI), Short Form (36) Health Survey (SF-36), Visual Analog Scale for Pain, and Visual Analog Scale for Itch.

3.3 Secondary Study Endpoints

To assess the safety, tolerability, and efficacy of topical gabapentin for 12 weeks in subjects with lymphocytic-type symptomatic scarring alopecia. Subjects will be followed up 4, 8, and 12 weeks during treatment with topical 6% gabapentin starting day 0 (Visit 2) and ending week 12 (Visit 5). Medication side effects, blood levels, and adverse experiences will be recorded.

3.4 Primary Safety Endpoints

A primary safety endpoint will take place when the first 5 subjects complete the study.

4 Subject Selection and Withdrawal

4.1 Inclusion Criteria

1. Male and female adults, greater than 18 years of age
2. Biopsy-proven diagnosis of primary scarring alopecia of lymphocytic inflammatory infiltrate type, indicated as one of the following conditions: lichen planopilaris, frontal fibrosing alopecia, or central centrifugal cicatricial alopecia
3. At least one persistent scalp symptom associated with inflammation: pain, burning, itch, tingling/crawling, stinging, or tenderness
4. Able to complete survey and questionnaire subjectively
5. Consents to participate in neurometer study and scalp biopsy acquisition
6. Willingness to adhere to study protocol
7. If subject is taking a neuromodulatory medication (including capsaicin cream, tricyclic antidepressants, carbamazepine, phenytoin, topiramate, oxcarbazepine, lamotrigine, morphine, Botox, etc), he or she must be a stable dose for at least 6 months prior to study enrollment

The gender of the subjects will not determine enrollment. There is no requirement of male to female ratio for this study. The age range of the subjects will be 18 years and older. No specific racial or ethnic restrictions will be present for this study. The FDA lists gabapentin as Pregnancy Category C: studies in animals have shown some harm to the fetus but its effects on human fetus are unknown due to limited data. It has not been found to be harmful during breastfeeding. Therefore, female subjects of childbearing potential will not be excluded since the drug will be topically administered with minimal systemic absorption.

4.2 Exclusion Criteria

1. Allergy or intolerance to gabapentin or the substances used in its compounding
2. Underlying disease that might be adversely affected by topical gabapentin
3. Application of topical immunomodulatory or immunosuppressive agent to the scalp in the preceding 2 weeks
4. Systemic administration of corticosteroid or other systemic treatment (i.e., methotrexate, phototherapy) that has immunomodulatory or other immunosuppressive mechanism of action, in the preceding 8 weeks

5. Clinical evidence of secondary skin infection
6. Individuals who have undergone scalp reduction surgery or hair transplantation
7. Asymptomatic disease
8. Immunosuppression due to disease state or use of systemic/topical biological agents (HIV, chemotherapy, immunomodulators, history of transplantation)
9. Any Investigational medications within the past 30 days, including those for migraines or scarring alopecias (anti-CGRP agents)
10. Use of GABAergic medications (including gabapentin and pregabalin) in the preceding 2 months
11. Use of illicit drugs or opioid medications
12. Evidence of anemia, thyroid disease, sarcoidosis or other medical condition that could impact hair growth and adversely impact the outcome of the study
13. Implantable Cardioverter Defibrillator (ICD) or pacemaker
14. Subject has any medical condition that, in the judgment of the Investigator, would jeopardize the subject's safety following exposure to the administered medications

If subjects are taking medications/treatments for their scarring alopecia at baseline visit, they will be asked to stop taking/administering them as described in the exclusion criteria.

4.3 Subject Recruitment and Screening

Subjects will be identified by the Principal Investigator, Dr. Maria K. Hordinsky. The study coordinator will assist in describing the study and answering questions.

Advertisements may be posted on the University of Minnesota campus and surrounding community. Advertising will be submitted to the Institutional Review Board (IRB) for approval before it is used. Language will also be submitted to the IRB so information about the study can be posted on our department website, as well distributed to the Cicatricial Alopecia Research Foundation.

In the screening process (Visit 1), subjects will be evaluated using the inclusion and exclusion criteria.

4.4 Early Withdrawal of Subjects

4.4.1 When and How to Withdraw Subjects

Participation in this study is voluntary. Subjects are free to withdraw at any time. Once initiated, individual subjects will receive enough gabapentin for 4 weeks at a time to administer. If withdrawn, subject will be asked to terminate use of the investigational drug and return the remaining gabapentin solution.

Investigators may withdraw subjects from the study if subjects fail to adhere to the study protocol requirements (e.g. use of other topical, oral or other medical treatments used for management of scarring alopecia during the study). Subjects may also be withdrawn if they experience an adverse reaction to the study medication or if their gabapentin blood levels exceed safety levels (>16 ug/mL).

4.4.2 Data Collection and Follow-up for Withdrawn Subjects

Data collection of withdrawn subjects will be collected up to the point of withdrawal. This data will still be included in the pool-data of the study for further analysis. Subjects who withdraw from further data collection will not be replaced with additional subjects.

If a subject withdraws consent to participate in the study, attempts will be made to obtain permission to record data up to the protocol-described end of subject follow-up period.

Three phone calls one week apart one from another will be made to the subjects lost to follow-up to record data up to the protocol-described end of subject follow-up period.

5 Study Drug

5.1 Description

Gabapentin is a GABA analogue anticonvulsant also used to treat neuropathic pain. It is thought to target voltage-gated calcium ion channels at pre- and post-synaptic membranes of neurons in the central and peripheral nervous system modulating the release of neurotransmitters.

Gabapentin is normally available in solid (powder) form and must be compounded into a topical solution. Based on published data of effective topical gabapentin preparation in vulvodynia and experience preparing topical gabapentin for use in patients with pain, IDS Pharmacy of University of Minnesota will compound the gabapentin into the solution for topical use. Once prepared, IDS will also be responsible for dispensing the solution of 6% gabapentin in an appropriate drug container to be given to subjects. Each subject participating in the study will receive enough gabapentin solution for use over four weeks, approximately a maximum of 2 mL a day; 60 mL for 4 weeks. After 4 weeks of treatment (Visit 4) and 8 weeks of treatment (Visit 5) the subject will return for follow up with the prescribed gabapentin container and will be given a new dispensed bottle of the solution for use during the next four weeks.

Treatment Regimen

Qualified subjects will be educated by the research coordinator on how to properly apply the gabapentin 6% solution two times daily onto intact skin of affected symptomatic scalp areas. The minimum and the maximum size of the scalp areas to be treated will be determined for each subject respectively, based on their disease pattern assessed during Visit 2. Treated sites will be initially recorded and should be treated for the entire 12 weeks unless the skin is adversely affected by the topical gabapentin.

Subjects may continue their normal grooming regimen as long as substances without other neuromodulatory agents or steroids are used during the treatment period. Recommended application will be in morning and evening at bedtime. The solution should be applied after hair washing if this coincides with time for application.

5.2 Method for Assigning Subjects to Treatment Groups

All participants will receive treatment with topical 6% gabapentin. The study design does not include a control group, therefore, randomization of participants will not occur.

5.3 Preparation and Administration of Study Drug

IDS will be responsible for the preparation and dispensing of gabapentin 6% solution to the principal investigators or clinical research coordinator (study team). The clinical research coordinator will provide subjects with the solution to administer two times daily after educating them on how to apply the drug. The gabapentin solution should be stored at room temperature (20° to 25°C)/(68° to 77°F) while always properly sealed and away from light and moisture. The study team will provide the subjects with a four week supply of solution at a time. Subjects will contact investigators or coordinator if they need more solution and will be asked to do so promptly if low on solution to avoid gaps in treatment.

5.4 Subject Compliance Monitoring

Subject participants will be informed that they will be asked to stop taking any medications/treatments for their scarring alopecia while participating in this study. This statement will be also written in the consent form that subjects will be asked to read, understand and sign prior participating in the study.

5.5 Prior and Concomitant Therapy

Subjects will be asked detailed information regarding their medical and medication history for general health issues and specific focused questions regarding their symptomatic scarring alopecia.

Subjects will not be allowed to use any medicines/therapies other than the gabapentin 6% solution on the scalp for their symptomatic scarring alopecia.

5.6 Packaging

The gabapentin 6% solution will be prepared through a compounding method by IDS Pharmacy and will be dispensed in red sealed containers with 60 mL of solution.

5.7 Blinding of Study Drug

This is not a blinded study.

5.8 Receiving, Storage, Dispensing and Return

5.8.1 Receipt of Drug Supplies

The Department of Dermatology Clinical Research Division will order 10 initial containers of 60 mL solution of gabapentin 6% solution from the IDS Pharmacy, University of Minnesota, Mayo Building, 2nd floor.

Upon receipt of the study treatment supplies, an inventory will be performed and a drug receipt log filled out and signed by the person accepting the shipment. It is important that the designated study staff counts and verifies that the shipment contains all the items noted in the shipment inventory. Any damaged or unusable study drug in a given shipment will be documented in the study files.

Prepared containers of gabapentin solution 6% will be kept at room temperature (20° to 25°C) away from moisture and light for up to 24 months at the IDS pharmacy, University of Minnesota, Phillips Wangensteen Building, 2nd floor.

5.8.2 Dispensing of Study Drug

IDS will dispense the drug-filled container to the investigators or coordinators. Once qualified to begin treatment, each subject will receive one container of 60 mL of gabapentin 6% solution from the clinical coordinator. Regular study drug reconciliation will be performed to document drug assigned. During follow-up visits, drug consumed and drug remaining will be recorded. This reconciliation will be logged on the drug reconciliation form, and signed and dated by the study team.

5.8.3 Return or Destruction of Study Drug

At the completion of the study, there will be a final reconciliation of drug dispensed, drug consumed, and drug remaining. This reconciliation will be logged on the drug reconciliation form, signed and dated. Any discrepancies noted will be investigated, resolved, and documented prior to return or destruction of unused study drug. Drug destroyed on site will be documented in the study files.

6 Study Procedures

6.1 Visit 1 (Screening/baseline)

Before any study-related procedures are performed, subjects will be screened for participation in the study using inclusion and exclusion criteria. Once determined to be a qualified candidate for participation, subjects will be asked to read and sign the consent form if they wish to participate in this research study. They will then be asked about their medical and medication history.

The following tests and procedures will be performed:

- Obtain medical history and medications
- Physical examination of scalp
- Lichen Planopilaris Activity Index (LPPAI) clinical assessment will be performed. Every effort will be made to have the same person evaluate the alopecia at each visit for any given subject.

- Scalp photography, especially affected areas that will be monitored and treated with gabapentin
- Subject to complete surveys to assess symptomatology pre-treatment: DLQI, SF-36, Pain VAS and Itch VAS
- Neurometer study to assess Aβ, Aδ, and C fiber function before gabapentin administration
- Collect four pre-treatment skin biopsy samples: two 4-mm biopsy specimens from affected scalp and two 4-mm biopsy specimens from normal-appearing scalp. Specimens will be analyzed for routine histology, confocal microscopic examination, and CGRP level.

If potential symptomatic subjects are currently taking medications/treatments for their scarring alopecia, they will be asked to stop the treatment as noted in the exclusion criteria in section 4.2.

6.2 Visit 2 (Day 0)

The following tests and procedures will be performed:

- Record adverse experiences
- Biopsy suture removal
- Review changes in medical history and medications since Visit 1
- LPPAI clinical assessment
- Scalp photography, especially affected areas that will be monitored and treated with gabapentin
- Subject to complete surveys to assess symptomatology pre-treatment: DLQI, SF-36, Pain VAS and Itch VAS
- Educate subject on how to apply topical gabapentin solution
- Provide subject with first container of gabapentin solution
- Subject begins treatment with topical gabapentin solution

6.3 Visit 3 (Week 4)

The following tests and procedures will be performed:

- Record adverse experiences
- Gabapentin blood level
- Review changes in medical history and medications since Visit 2
- LPPAI clinical assessment
- Subject to complete surveys to assess symptomatology: DLQI, SF-36, Pain VAS and Itch VAS
- Collect and assess first container of gabapentin solution
- Provide subject with new container of gabapentin solution

Subject has now completed four weeks of topical gabapentin therapy. Answer any questions/concerns subject has about drug application and collect feedback on ease of use and/or impact on grooming practices.

6.4 Visit 4 (Week 8)

The following tests and procedures will be performed:

- Record adverse experiences
- Gabapentin blood level
- Review changes in medical history and medications since Visit 3
- LPPAI clinical assessment
- Subject to complete surveys to assess symptomatology: DLQI, SF-36, Pain VAS and Itch VAS
- Collect and assess second container of gabapentin solution
- Provide subject with new container of gabapentin solution

Subject has now completed eight weeks of topical gabapentin therapy. Answer any questions/concerns subject has about drug application and collect feedback on ease of use and/or impacting on grooming practices.

6.5 Visit 5 (Week 12)

The following tests and procedures will be performed:

- Record adverse experiences
- Physical examination of scalp
- Gabapentin blood level
- Review changes in medical history and medications since Visit 4
- LPPAI clinical assessment
- Scalp photography, especially affected areas that are being monitored and treated with gabapentin
- Subject to complete surveys to assess symptomatology: DLQI, SF-36, Pain VAS and Itch VAS
- Neurometer study to assess Aβ, Aδ, and C fiber function after gabapentin administration
- Collect and assess third container of gabapentin solution
- Collect four post-treatment skin biopsy samples: two 4-mm skin biopsy specimens from affected scalp and two 4-mm biopsy specimens from normal-appearing scalp. Specimens will be analyzed for routine histology, confocal microscopic examination, and CGRP level.

Subject has now completed the entire twelve weeks of topical gabapentin therapy.

6.6 Visit 6 (2 week follow-up)

The following tests and procedures will be performed:

- Record adverse experiences
- Review changes in medical history and medications since Visit 5
- LPPAI clinical assessment
- Subject to complete surveys to assess symptomatology: DLQI, SF-36, Pain VAS and Itch VAS
- Biopsy suture removal

A flowchart of the study can be found in Section 3.1 General Design.

7 Statistical Plan

7.1 Sample Size Determination

This is a pilot study with the plan to enroll 10 subjects. The reasoning for sample size selection is to proceed with preliminary studies in a small group. All subjects will be selected based on inclusion and exclusion criteria.

7.2 Statistical Methods

An intent-to-treat analysis will be performed in all subjects for symptoms and sign scores comparing the last treatment visit to baseline. A combination of methods will be included for analysis. Descriptive statistics including either numerically or graphical representations to summarize the data will be used.

7.3 Subject Population(s) for Analysis

Data collected from all subjects will be included for the analysis. Data collection of withdrawn subjects will be collected up to the point of withdrawal. This data will still be included in the pool-data of the study for further analysis.

8 Safety and Adverse Events

8.1 Definitions

Adverse Event

An ***adverse event*** (AE) is any symptom, sign, illness or experience that develops or worsens in severity during the course of the study. Intercurrent illnesses or injuries should be regarded as adverse events. Abnormal results of diagnostic procedures are considered to be adverse events if the abnormality:

- results in study withdrawal
- is associated with a serious adverse event
- is associated with clinical signs or symptoms
- leads to additional treatment or to further diagnostic tests
- is considered by the investigator to be of clinical significance

Serious Adverse Event

Adverse events are classified as serious or non-serious. A ***serious adverse event*** is any AE that is:

- fatal
- life-threatening
- requires or prolongs hospital stay
- results in persistent or significant disability or incapacity
- a congenital anomaly or birth defect
- an important medical event

Important medical events are those that may not be immediately life threatening, but are clearly of major clinical significance. They may jeopardize the subject, and may require intervention to prevent one of the other serious outcomes noted above. For example, drug overdose or abuse, a seizure that did not result in in-patient hospitalization, or intensive treatment of bronchospasm in an emergency department would typically be considered serious.

All adverse events that do not meet any of the criteria for serious will be regarded as ***non-serious adverse events***.

Adverse Event Reporting Period
The study period during which adverse events must be reported is normally defined as the period from the initiation of any study procedures to the end of the study treatment follow-up. For this study, the study treatment follow-up is defined as 14 weeks following the start of administration of study treatment (Day 0).

Preexisting Condition
A preexisting condition is one that is present at the start of the study. A preexisting condition will be recorded as an adverse event if the frequency, intensity, or the character of the condition worsens during the study period.

General Physical Examination Findings
At screening, any clinically significant abnormality will be recorded as a preexisting condition. At the end of the study, any new clinically significant findings/abnormalities that meet the definition of an adverse event will also be recorded and documented as an adverse event.

Post-study Adverse Event
All unresolved adverse events will be followed by the investigator until the events are resolved, the subject is lost to follow-up, or the adverse event is otherwise explained. At the last scheduled visit, the investigator will instruct each subject to report any subsequent event(s) that the subject, or the subject's personal physician, believes might reasonably be related to participation in this study.

Abnormal Laboratory Values
Gabapentin blood levels will be monitored to ensure gabapentin toxicity does not occur. If gabapentin levels reach or exceed 16 ug/mL, gabapentin treatment will be interrupted. Abnormal gabapentin levels will be recorded as an adverse event and followed by the investigator until the event has resolved.

Hospitalization, Prolonged Hospitalization or Surgery
Any adverse event that results in hospitalization or prolonged hospitalization will be documented and reported as a serious adverse event unless specifically instructed otherwise in this protocol. Any condition responsible for surgery will be documented as an adverse event if the condition meets the criteria for an adverse event.

Neither the condition, hospitalization, prolonged hospitalization, nor surgery are reported as an adverse event in the following circumstances:

- Hospitalization or prolonged hospitalization for diagnostic or elective surgical procedures for a preexisting condition. Surgery should ***not*** be reported as an outcome of an adverse event if the purpose of the surgery was elective or diagnostic and the outcome was uneventful.
- Hospitalization or prolonged hospitalization required to allow efficacy measurement for the study.
- Hospitalization or prolonged hospitalization for therapy of the target disease of the study, unless it is a worsening or increase in frequency of hospital admissions as judged by the clinical investigator.

8.2 Recording of Adverse Events

At each contact with the subject, the investigators will seek information on adverse events by specific questioning and, as appropriate, by examination. Information on all adverse events will be recorded immediately in the source document, and also in the appropriate adverse event module of the case report form (CRF). All clearly related signs, symptoms, and abnormal diagnostic procedures results will be recorded in the source document, though will be grouped under one diagnosis.

All adverse events occurring during the study period will be recorded. The clinical course of each event will be followed until resolution, stabilization, or until it has been determined that the study treatment or participation is not the cause. Serious adverse events that are still ongoing at the end of the study period will be followed up to determine the final outcome. Any serious adverse event that occurs after the study period and is considered to be possibly related to the study treatment or study participation will be recorded and reported immediately.

8.3 Reporting of Serious Adverse Events

8.3.1 Study Sponsor Notification by Investigator

A Serious Adverse Event (SAE) form will be completed by the investigator within 24 hours. The investigator will keep a copy of this SAE form on file at the study site. Report serious adverse events by phone and facsimile to:

Maria K. Hordinsky, MD
Cell: 612-710-5507
Fax: 612-624-6678

At the time of the initial report, the following information should be provided:

- Study identifier
- Study Center
- Subject number
- A description of the event
- Date of onset
- Current status
- Whether study treatment was discontinued
- The reason why the event is classified as serious
- Investigator assessment of the association between the event and study treatment

Within the following 48 hours, the investigator will provide further information on the serious adverse event in the form of a written narrative. This should include a copy of the completed Serious Adverse Event form, and any other diagnostic information that will assist the understanding of the event. Significant new information on ongoing serious adverse events will be provided promptly to the principal investigator, Maria K. Hordinsky, and Department of Dermatology.

8.3.2 IRB Notification by Investigator

Reports of all serious adverse events (including follow-up information) will be submitted to the IRB within 10 working days if it falls under the UPIRTSO guidelines. Copies of each report and documentation of IRB notification and receipt will be kept in the Clinical Investigator's binder.

8.3.3 FDA Notification by Sponsor

The study sponsor shall notify the FDA by telephone or by facsimile transmission of any unexpected fatal or life-threatening experience associated with the use of the drug as soon as possible but no later than 7 calendar days from the investigator's original receipt of the information.

If a previous adverse event that was not initially deemed reportable is later found to fit the criteria for reporting, the investigators will submit the adverse event in a written report to the FDA as soon as possible, but no later than 15 calendar days from the time the determination is made.

8.4 Unblinding Procedures

This is not a blinded study.

8.5 Stopping Rules

Individual subjects will be administering topical gabapentin independently without supervision by study team. Subjects are to terminate treatment if any new adverse symptoms different from before treatment occur or worsen and contact the study team immediately. Individual subjects will also be asked to terminate treatment if their gabapentin blood levels are >16 ug/mL.

8.6 Medical Monitoring

It is the responsibility of the Principal Investigator to oversee the safety of the study at his/her site. This safety monitoring will include careful assessment and appropriate reporting of adverse events as noted above, as well as the construction and

implementation of a site data and safety-monitoring plan (see section 10 Auditing, Monitoring and Inspecting). Medical monitoring will include a regular assessment of the number and type of serious adverse events.

9 Data Handling and Record Keeping

9.1 Confidentiality

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Those regulations require a signed subject authorization informing the subject of the following:

- What protected health information (PHI) will be collected from subjects in this study
- Who will have access to that information and why
- Who will use or disclose that information
- The rights of a research subject to revoke their authorization for use of their PHI

In the event that a subject revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. For subjects that have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (i.e. that the subject is alive) at the end of their scheduled study period.

9.2 Source Documents/Case Report Forms

Source data for this study include subject's medical records, , surveys (DLQI, SF-36, Pain VAS, Itch VAS), photographs, neurometer study data, biopsy pathology reports, gabapentin level lab reports, ELISA CGRP level reports, pharmacy dispensing records, confocal microscopy photographs, and subject files.

Data generated by the methods described in the protocol will be recorded in the subjects' medical records and/or study progress notes. Data may be transcribed legibly on CRFs supplied for each subject or directly inputted into an electronic system or any combination thereof.

9.3 Records Retention

Investigators will retain study essential documents for at least 2 years after the formal discontinuation of the study. The documents will be locked and stored in the clinical research office space.

10 Study Auditing, and Inspecting

10.1 Auditing and Inspecting

The investigator will permit study-related monitoring, audits, and inspections by the IRB, the sponsor, government regulatory bodies, and University compliance and quality

assurance groups of all study related documents (e.g. source documents, regulatory documents, data collection instruments, study data etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g. pharmacy, diagnostic laboratory, etc.).

Participation as an investigator in this study implies acceptance of potential inspection by government regulatory authorities and applicable University compliance and quality assurance offices.

11 Ethical Considerations

This study is to be conducted according to US and international standards of Good Clinical Practice (FDA Title 21 part 312 and International Conference on Harmonization guidelines), applicable government regulations and Institutional research policies and procedures.

This protocol and any amendments will be submitted to a properly constituted independent Institutional Review Board (IRB), in agreement with local legal prescriptions, for formal approval of the study conduct. The decision of the IRB concerning the conduct of the study will be made in writing to the investigator and a copy of this decision will be provided to the sponsor before commencement of this study.

All subjects for this study will be provided a consent form describing this study and providing sufficient information for subjects to make an informed decision about their participation in this study. The consent form will be submitted with the protocol for review and approval by the IRB for the study. The formal consent of a subject, using the IRB-approved consent form, will be obtained before that subject is submitted to any study procedure. This consent form will be signed by the subject or legally acceptable surrogate, and the investigator-designated research professional obtaining the consent.

12 Study Finances

12.1 Funding Source

The Cicatricial Alopecia Research Foundation will fund the treatment portion of the study. The Department of Dermatology Clinical Research Division, University of Minnesota, will fund the biopsy portion of the study with internal funding. Subjects and/or their insurance companies will not be charged for study-related procedures or visits.

12.2 Research Related Injury

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to the subject or the subject's insurance company.

12.3 Subject Stipends or Payments

Subjects will receive $25.00 for each biopsy obtained as part of the study. Payment will be provided in the form of a gift card after acquisition of the scalp biopsies at Visits 1 and 5.

12.4 Conflict of Interest

The investigators have no conflict of interest.

Any investigator who has a conflict of interest with this study (patent ownership, royalties, or financial gain greater than the minimum allowable by their institution, etc.) will refer to the Regents Policies on Individual Conflict of Interest Policy or Institutional Conflict of Interest Policy. These policies require University Faculty and staff to report external professional activities and business and significant financial interests related to his or her University activities by submitting a REPA (Report of External Professional Activities) at least once per year. Faculty and staff will also file a REPA when substantial changes in business or financial interests occur, when an activity that presents a potential conflict of interest is anticipated, or when submitting an application for research support or technology transfer, submitting research protocols to the IRB, or receiving financial contributions. All University of Minnesota investigators will follow the University conflict of interest policy.

13 Publication Plan

Maria Hordinsky, MD holds the primary responsibility for publication of any results of the study. Other investigators must first obtain approval from the primary responsible party before any information may be used or passed on to a third party.

14 References

1. Harries MJ, Sinclair RD, MacDonald-Hull S, Whiting DA, Griffiths CEM, Paus R. Management of primary cicatricial alopecias: options for treatment. Br J Dermatol, 2008 Jul; 159 (1):1-22.

2. Hainline B. Chronic pain: physiological, diagnostic, and management considerations. Psychiatr Clin N Am, 2005; 28: 713–735.

3. Wacnik PW, Baker CM, Herron MJ, Kren BT, Blazar BR, Wilcox GL, Hordinsky MK, Beitz AJ, Ericson ME. Tumor-induced mechanical hyperalgesia involves CGRP receptors and altered innervation and vascularization of DsRed2 fluorescent hindpaw tumors. Pain, 2005 May;115(1-2):95-106.4).

4. Durham PL. Inhibition of calcitonin gene-related peptide function: a promising strategy for treating migraine. Headache, 2008 Sep; 48(8):1269-75.

5. Boardman LA, Cooper AS, Blais LR, Raker CA. Topical gabapentin in the treatment of localized and generalized vulvodynia. Obstetrics and Gynecology 2008 Sep; 112(3):579-585.

6. Vuković V, Lovrencić-Huzjan A, Bosnar-Puretić M Demarin V. The efficacy of gabapentin in migraine prophylaxis: an observational open label study. Acta Clin Croat 2009 Jun;48(2):145-51.

7. Hamada J. Use of antiepileptic drugs for the preventive treatment of migraine. Brain Nerve. 2009 Oct;61(10):1117-24

8. Chiang C, Sah D, Cho B, Ochoad BE, Price VH. Hydroxychloroquine and lichen planopilaris: Efficacy and introduction of Lichen Planopilaris Activity Index scoring system. J Amer Acad Dermatol 2010; 62(3): 387-392.

9. Olsen EA, Bergfeld WF, Cotsarelis G, Price VH, Shapiro J, Sinclair R, Solomon A, Sperling L, Stenn K, Whiting DA. Summary of North American Hair Research Society (NAHRS) - sponsored workshop on cicatricial alopecia, Duke University Medical Center, F. J Amer Acad Dermatol 2003; 48:103-10.

15 Attachments

Appendix A: Dermatology Life Quality Index (DLQI)
Appendix B: Short Form (36) Health Survey (SF-36)
Appendix C: Visual Analog Scale (VAS) for pain
Appendix D: Visual Analog Scale (VAS) for itch
Appendix E: Lichen Planopilaris Activity Index (LPPAI)
Appendix F: Adverse Event Report Form

Appendix A: Dermatology Quality of Life Index (DLQI)

DERMATOLOGY LIFE QUALITY INDEX

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please tick ❒ one box for each question.

1.	Over the last week, how **itchy**, **sore**, **painful** or **stinging** has your skin been?	Very much A lot A little Not at all	❒3 ❒2 ❒1 ❒0
2.	Over the last week, how **embarrassed** or **self-conscious** have you been because of your skin?	Very much A lot A little Not at all	❒3 ❒2 ❒1 ❒0
3.	Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home** or **garden**?	Very much A lot A little Not at all Not relevant	❒3 ❒2 ❒1 ❒0 ❒0
4.	Over the last week, how much has your skin influenced the **clothes** you wear?	Very much A lot A little Not at all Not relevant	❒3 ❒2 ❒1 ❒0 ❒0
5.	Over the last week, how much has your skin affected any **social** or **leisure** activities?	Very much A lot A little Not at all Not relevant	❒3 ❒2 ❒1 ❒0 ❒0
6.	Over the last week, how much has your skin made it difficult for you to do any **sport**?	Very much A lot A little Not at all Not relevant	❒3 ❒2 ❒1 ❒0 ❒0
7.	Over the last week, has your skin prevented you from **working** or **studying**?	Yes No Not relevant	❒3 ❒ ❒0
	If "No", over the last week how much has your skin been a problem at **work** or **studying**?	A lot A little Not at all	❒2 ❒1 ❒0

Page 1 score _____

8.	Over the last week, how much has your skin created problems with your **partner** or any of your **close friends** or **relatives**?	Very much A lot A little Not at all Not relevant	❒3 ❒2 ❒1 ❒0 ❒0
9.	Over the last week, how much has your skin caused any **sexual difficulties**?	Very much A lot A little Not at all Not relevant	❒3 ❒2 ❒1 ❒0 ❒0
10.	Over the last week, how much of a problem has the **treatment** for your skin been, for example by making your home messy, or by taking up time?	Very much A lot A little Not at all Not relevant	❒3 ❒2 ❒1 ❒0 ❒0

Please check you have answered EVERY question. Thank you.

Page 2 score _____

Page 1 score _____ + Page 2 score _____ = Total DLQI score _____

Appendix B: Short Form (36) Health Survey (SF-36)

RAND 36-Item Health Survey 1.0 Questionnaire Items

1. In general, would you say your health is:
   - ☐1 Excellent
   - ☐2 Very Good
   - ☐3 Good
   - ☐4 Fair
   - ☐5 Poor

2. **Compared to one year ago,** how would you rate your health in general **now**?
   - ☐1 Much better now than one year ago
   - ☐2 Somewhat better now than one year ago
   - ☐3 About the same
   - ☐4 Somewhat worse now than one year ago
   - ☐5 Much worse now than one year ago

The following items are about activities you might do during a typical day. Does **your health now limit you** in these activities? If so, how much?

(Check one number on each line)

	Yes, Limited a Lot ✓	Yes, Limited a Little ✓	No, Not limited at All ✓
3. **Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports	☐1	☐2	☐3
4. **Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐1	☐2	☐3
5. Lifting or carrying groceries	☐1	☐2	☐3
6. Climbing **several** flights of stairs	☐1	☐2	☐3
7. Climbing **one** flight of stairs	☐1	☐2	☐3
8. Bending, kneeling, or stooping	☐1	☐2	☐3
9. Walking **more than a mile**	☐1	☐2	☐3
10. Walking **several blocks**	☐1	☐2	☐3
11. Walking **one block**	☐1	☐2	☐3
12. Bathing or dressing yourself	☐1	☐2	☐3

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health**?

(Check One Number on Each Line)

	Yes ✓	No ✓
13. Cut down the amount of time you spent on work or other activities	☐1	☐2
14. **Accomplished less** than you would like	☐1	☐2
15. Were limited in the **kind** of work or other activities	☐1	☐2
16. Had **difficulty** performing the work or other activities (for example, it took extra effort)	☐1	☐2

During the **past 4 weeks,** have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

(Check One Number on Each Line)

	Yes ✓	No ✓
17. Cut down the **amount of time** you spent on work or other activities	☐1	☐2
18. **Accomplished less** than you would like	☐1	☐2
19. Didn't do work or other activities as **carefully** as usual	☐1	☐2

20. During the **past 4 weeks,** to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups? **(Check One Number)**

☐1 Not at all
☐2 Slightly
☐3 Moderately
☐4 Quite a bit
☐5 Extremely

21. How much **bodily** pain have you had during the **past 4 weeks?**
(Check One Number)

☐1 None
☐2 Very mild
☐3 Mild
☐4 Moderate
☐5 Severe
☐5 Very severe

22. During the **past 4 weeks,** how much did **pain** interfere with your normal work (including both work outside the home and housework)?
(Check One Number)

☐1 Not at all
☐2 A little bit
☐3 Moderately
☐4 Quite a bit
☐5 Extremely

These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the **past 4 weeks** . . .

(Check One Number on Each Line)

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	None of the Time
23. Did you feel full of pep?	☐1	☐2	☐3	☐4	☐5	☐6
24. Have you been a very nervous person?	☐1	☐2	☐3	☐4	☐5	☐6
25. Have you felt so down in the dumps that nothing could cheer you up?	☐1	☐2	☐3	☐4	☐5	☐6
26. Have you felt calm and peaceful?	☐1	☐2	☐3	☐4	☐5	☐6

27. Did you have a lot of energy?	☐1	☐2	☐3	☐4	☐5	☐6
28. Have you felt downhearted and blue?	☐1	☐2	☐3	☐4	☐5	☐6
29. Did you feel worn out?	☐1	☐2	☐3	☐4	☐5	☐6
30. Have you been a happy person?	☐1	☐2	☐3	☐4	☐5	☐6
31. Did you feel tired?	☐1	☐2	☐3	☐4	☐5	☐6

32. During the **past 4 weeks,** how much of the time has your **physical health or emotional problems** interfered with your social activities (like visiting with friends, relatives, etc.)?

(Check One Number)

☐1 All of the time
☐2 Most of the time
☐3 Some of the time
☐4 A little of the time
☐5 None of the time

How TRUE or FALSE is <u>each</u> of the following statements for you.

(Circle One Number on Each Line)

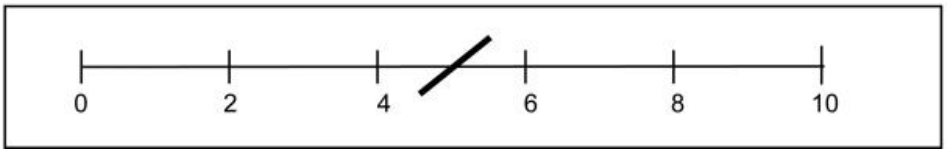
	Definitely True ✓	Mostly True ✓	Don't Know ✓	Mostly False ✓	Definitely False ✓
1. I seem to get sick a little easier than other people	☐1	☐2	☐3	☐4	☐5
2. I am as healthy as anybody I know	☐1	☐2	☐3	☐4	☐5
3. I expect my health to get worse	☐1	☐2	☐3	☐4	☐5
4. My health is excellent	☐1	☐2	☐3	☐4	☐5

RAND-36 score: _____

Appendix C: Itch Visual Analog Scale (VAS)

Draw a line anywhere on the scale that best represents the severity of your itching:

Example:



Appendix D: Pain Visual Analog Scale (VAS)

Draw a line anywhere on the scale that best represents the severity of your pain:

Appendix E: Lichen Planopilaris Activity Index (LPPAI)

A. Pruritis	❒ 0	❒ 1	❒ 2	❒ 3
B. Pain	❒ 0	❒ 1	❒ 2	❒ 3
C. Burning	❒ 0	❒ 1	❒ 2	❒ 3
D. Erythema	❒ 0	❒ 1	❒ 2	❒ 3
E. Perifollicular erythema	❒ 0	❒ 1	❒ 2	❒ 3
F. Perifollicular scale	❒ 0	❒ 1	❒ 2	❒ 3
Pull test	❒ Positive	❒ Negative		
Spreading	❒ Yes	❒ No		
Crusting	❒ Yes	❒ No		
Pustules	❒ Yes	❒ No		
Dimensions/extent	❒ Yes	❒ No		
Loss follicular markings	❒ Yes	❒ No		
Tufting	❒ Yes	❒ No		
Telangiectasia	❒ Yes	❒ No		
Atrophy	❒ Yes	❒ No		
Pigment change	❒ Yes	❒ No		
Other skin, nail, mucous membrane	❒ Yes	❒ No		

Scale:
0 = negative
1 = + / -
2 = +
3 = ++,+++

Positive/Yes = 1
Negative/No = 0

LPPAI score = (A+B+C+D+E+F)/3 + 2.5(pull test) + 1.5(spread/2)

Appendix F: Adverse Event Report Form

Subject ID: ☐☐☐☐☐

Subject initials: ☐☐☐

This form is a tool for study personnel to track adverse events. Adverse events need to be summarized at the time of annual IRB renewal. All sections may be filled out by the principal investigator or co-investigators.

A. Adverse Event Description:

❒ Medication ❒ Blood Draw ❒ Other _____

B. Date & Time of Adverse Event:

Start Date: ☐☐ / ☐☐ / ☐☐ Start Time: ☐☐ : ☐☐

End Date: ☐☐ / ☐☐ / ☐☐ End Time: ☐☐ : ☐☐

C. Treatment Needed? ❒ Yes ❒ No

If yes, describe: _____

D. Outcome of the Experience:

❒ Resolved ❒ Continuing ❒ Death

E. Severity of Experience: Grade ❒ 1 ❒ 2 ❒ 3 ❒ 4 ❒ 5

Severity Scale ❒ CTCAE ❒ Other _____

F. Was this a serious event? ❒ Yes ❒ No

G. Was the event unanticipated? ❒ Yes ❒ No

H. Was the event related to study procedures?

❒ Definitely ❒ Probably ❒ Possibly ❒ Unlikely ❒ Unrelated

If yes to F-H, report to IRB as a UPIRTSO.

G. Was this event recorded on AE log? ❒ Yes ❒ No

Additional Comments: