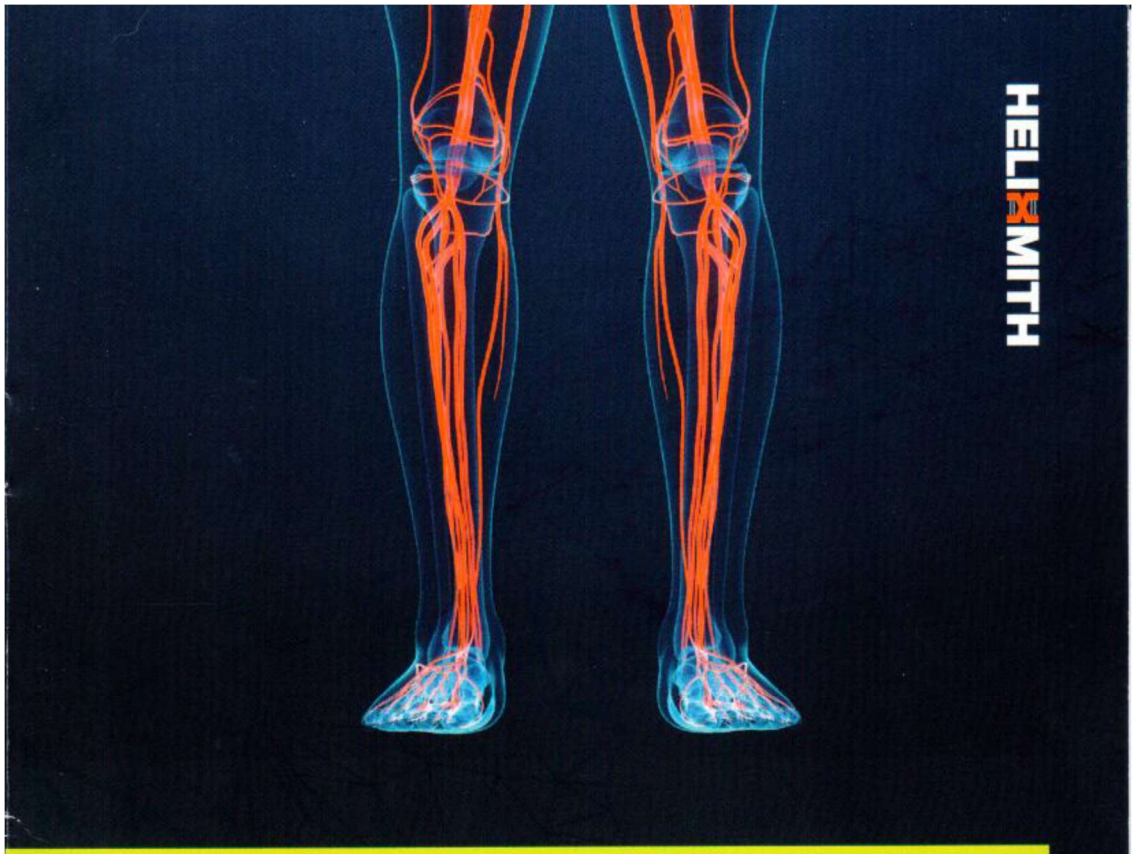

HELIXMITH

YOUR GUIDE TO THE REGAiN-1A STUDY

A Clinical Study for People with Painful Diabetic Peripheral Neuropathy

REGAiN-1A

What is a clinical study?

Clinical studies play an important role in the development of future medical treatments. They are designed to evaluate investigational treatments for their overall safety and effectiveness. Clinical studies are performed according to government regulations that protect the safety and rights of study participants.

Regulatory agencies have created strict, specific rules for conducting clinical studies. For example, all clinical studies must be approved and monitored by an Institutional Review Board or Ethics Committee, whose role is to protect all participants in a clinical study. All personal information provided by study participants is kept confidential.

What is informed consent?

Every patient who considers participating in a clinical study takes part in the informed consent process. During this process, the clinical study – including the study design, tests and procedures, and possible benefits and risks – is explained in detail. Any questions that a patient may have during this process are answered by the study team. The study-related information discussed during this process is included in the Informed Consent Form.

The informed consent process ensures that patients fully understand what study participation means. It also helps patients decide whether or not to participate. Participation is always voluntary; patients only participate in clinical studies if they want to, and they can stop participating at any time, for any reason. Your decision to participate – or to not participate – will have no effect on the medical care you receive now or in the future.

An Overview of the REGAiN-1A Study

The REGAiN-1A Study is a clinical study designed to evaluate the safety and effectiveness of an investigational drug (Engensis) in patients with painful DPN. The goal is to see what effect Engensis has on reducing pain in the feet and lower legs. It will be compared to a placebo, which is an inactive substance that has no effect on painful DPN.

This study is "double-blinded," meaning that you and the study doctor will not know which treatment you are receiving. All study participants will be randomly assigned (50/50 chance) to one of two treatment groups:

- Engensis Group: If you are assigned to this group, you will receive injections of 32 mg of Engensis over the course of four visits. At each visit, you will receive a total of 16 injections into each calf with a very fine needle.
- Placebo Control Group: If you are assigned to this group, you will receive a sterile saline solution without any active ingredients, rather than Engensis, using the identical injection technique. This group will receive the same number of injections as the Engensis Group.

Study Participation At-A-Glance

Participation in this clinical study will last approximately 6 months and is made up of the following periods:

Screening Period:

- 52 Days Prior to Enrollment: Tests and assessments will be given to determine your eligibility. During this period, you will be asked to keep a 7-day pain diary.

First Treatment Cycle:

- Day 0: First injection visit. You will receive your assigned study drug.
- Day 14: Second injection visit. You will receive your assigned study drug.

Two Follow-up Visits:

- Days 28 and 60: Tests and assessments to monitor your condition.

Second Treatment Cycle:

- Day 90: Third injection visit. You will receive your assigned study drug.
- Day 104: Fourth injection visit. You will receive your assigned study drug.

Follow-up Visit:

- Day 150: Tests and assessments to monitor your condition.

End of Study Visit:

- Day 180: You will be asked to complete a 7-day pain diary prior to this visit. This visit will include tests and assessments to monitor your condition.
- You will be required to keep a pain diary. It is important that you provide accurate and consistent data.

Rescue Pain Medication During Study Participation

While you are participating in this clinical study, you will be given an electronic diary to record various items. One of them is to document the need to take an additional medication – acetaminophen 500 mg – for pain.

- You will be allowed to take 2 caplets every 6 hours as needed.
- You are allowed a maximum of 6 caplets (3000 mg) each day.
- It is important to only use this bottle of acetaminophen for DPN pain and not for other pain or medical conditions.
- Every time you take acetaminophen, you will record on the electronic diary provided your pain level before use, the date and time of use, and the amount of acetaminophen used.
- At each visit, you will return the diary and the bottles of acetaminophen even if you have not taken any.
- The study team will count how many caplets you have taken between visits and will dispense additional bottles of acetaminophen if needed.

NOTE

You should not take any other products that have acetaminophen during the study unless it is for something other than your DPN pain.

Medication Use During Your Study Participation

Prior to your participation in this clinical study, the study doctor will review the medications you are currently taking. There are some restrictions on what medications are allowed during the study. The study doctor will review the following with you in detail:

- You will not be allowed to take Lyrica or Neurontin at any time during your participation in this study.
- If you are already taking Cymbalta, other antidepressants or any antiepileptics (e.g., valproic acid, carbamazepine, vigabatrin), you should continue to take them. You must agree to not start or stop these medications during the study.
  - If you are taking these medications when you begin participating in this study, you must stay on a stable dose.
- The following therapies are <u>not allowed</u> during the study:
  - Skeletal muscle relaxants
  - Opioids (except after trauma or surgery)
  - Acupuncture
  - TENS
  - Injectable or oral steroids
  - Benzodiazepines (except for stable bedtime dose)
  - Capsaicin (to lower legs and feet)
  - Local anesthetic creams (except for local topical anesthetic cream applied immediately prior to study drug injections by the study doctor or nurse doing the procedure)
  - Anesthetic patches
  - Isosorbide dinitrate (ISDN) spray applied to the lower legs or feet