# EPPIC-Net: Platform Protocol to Assess Treatments for Painful Diabetic Peripheral Neuropathy

**Status:** RECRUITING

## Eligibility Criteria

**Age:** 18 years and over

This study is NOT accepting healthy

**Healthy Volunteers:** volunteers

3.1. Platform Protocol Inclusion Criteria (To be used in conjunction with ISA-specific criteria. Note, some ISA criteria may be more stringent than Platform criteria; always follow the more stringent criteria when determining eligibility.) Participants must meet all of the following inclusion criteria: 1. Able to provide informed consent. Legally Authorized Representatives (LARs) are not allowed, but impartial witnesses may be utilized as needed for visually impaired participants. 2. 18 years of age and older 3. Diagnosis of diabetes mellitus 4. Meets the Toronto Criteria for probable clinical sensorimotor polyneuropathy, with PDPN symptoms present for at least six months. This is defined as a combination of symptoms and signs with any two or more of the following (must be present bilaterally in the distal lower extremities): neuropathic symptoms, decreased distal sensation, or unequivocally decreased (or absent) ankle reflexes. Specifically: 1. The presence of any neuropathic symptoms on either the "Douleur Neuropathique en 4 Questions" (DN4) or the EPPIC-Net Neuropathy Exam will suffice to demonstrate "neuropathic symptoms." 2. Decreased distal sensation is satisfied by any of the following: i. "Yes" is checked at least once under Question 3 of the DN4 which queries hypoesthesia to touch and pinprick. ii. At least one score of "reduced" or "absent" on the right AND at least one score of "reduced" or "absent" on the left in any of the following items from the EPPIC-Net Neuropathy Exam: * Pin sensation in segments 1 or 2 (i.e. the toes and feet) * Vibration at the great toe * Joint position at the great toe * Light touch/touch pressure at the great toe * Temperature at the great toe * Monofilament at the great toe c. Decreased or absent ankle reflexes is satisfied by a score of "reduced" or "absent" on the right AND left in the "Ankle reflex" item in the EPPIC-Net Neuropathy Exam. 5. A score of at least 4 on the "Douleur Neuropathique en 4 Questions" (DN4). 6. Pain reporting during a pre-defined 7-day screening period meets study criteria (to be established using a centrally-administered screening algorithm) which may account for mean pain intensity reported, variability in reported values, and adherence in reporting. 7. Patient reported daily 11-point NRS (for average and worst pain over the last 24 hours) is completed on at least 5 out of the 7 days in the screening and baseline periods. 8. Participants must be willing and able to comply with scheduled visits, the treatment schedule, laboratory testing, and other requirements of the study (e.g., completion of app-based daily reporting). 9. Females may be included if they meet at least one of the following criteria (note that individual ISAs may specify more stringent measures to prevent pregnancy): a. Are not of childbearing potential, defined as one or more of the following: i. Post-menopausal for at least 1 year ii. Surgically sterile (bilateral tubal ligation, bilateral oophorectomy, or hysterectomy) iii. XY genotype iv. Turner syndrome v. Uterine agenesis. b. Are completely abstinent from sexual activity capable of resulting in pregnancy (as part of their preferred and usual lifestyle). This will include females whose sole sexual partner is a male who has undergone surgical sterilization or vasectomy. c. Women of childbearing potential will agree to practice an effective form of two types of birth control, which are defined as those, alone or in combination, that result in a low failure rate (i.e., less than 1% per year) when used consistently and correctly. This must be done before, throughout, and for 30 days after the last dose of DB study drug. Acceptable methods are: i. Hormonal methods such as the vaginal ring, or oral, implantable, injectable, or transdermal contraceptives for a minimum of 1 full cycle (based on the participant's usual menstrual cycle period) before study drug administration. ii. Intrauterine device. iii. Barrier method of contraception: condoms with or without a spermicidal agent, diaphragm or cervical cap with spermicide 10. Specific requirements of male participants (regarding contraception) will be defined in the ISAs based on the potential toxicity profile of the asset. 3.2. Platform Protocol Exclusion Criteria (To be used in conjunction with ISA-specific criteria; note, some ISA criteria may be more stringent than Platform criteria; always follow the more stringent criteria when determining eligibility) Please note that some of the below criteria which depend on clinical judgment require contacting the MM. Participants must not meet any of the following exclusion criteria, organized by category: 3.2.1. Neuropathy Confound Exclusion Criteria 1. Peripheral neuropathy that is known to have been caused by a condition other than diabetes (e.g. HIV, cancer/chemotherapy-induced, other medication-induced, alcohol-induced, hereditary, autoimmune neuropathies, uncontrolled or untreated hypothyroidism). Note that participants will not be tested for HIV, this will be established by patient report or review of the medical record. 2. Other significant pain conditions involving the same area as the neuropathy (e.g. physical deformity of the feet, plantar fasciitis, lumbosacral radiculopathy with distal lower extremity pain, fibromyalgia involving the lower limbs, Morton's neuroma), that in the opinion of the investigator would interfere with the participant's ability to rate the neuropathy pain. 3. Other pain conditions not involving the same area as the neuropathy which (in the opinion of the investigator) interfere with the participant's ability to rate the neuropathy pain. 4. Any amputation of the lower limb which interferes with the participant's ability to rate the neuropathy pain. If there is any amputation please contact the MM to confirm eligibility prior to randomization to an ISA. 5. The presence of any current foot ulcer. 6. Significant peripheral vascular disease defined as symptoms consistent with intermittent claudication. 3.2.2. Medication/Treatment Exclusion Criteria 7. Use of other investigational drugs within 3 months before screening and throughout the study. 8. Known or suspected hypersensitivity to all of the assets (active component and excipients) currently being tested in the Platform Protocol. 9. Undergone neurolytic or neurosurgical therapy or used an implanted neurostimulating device for neuropathic pain in the distal lower limbs within 3 months of screening. 10. Use of the high dose capsaicin patch (8%) in the 6 months before screening and throughout the study (for the treatment of PDPN). Use of the capsaicin patch in a manner that is not expected to interfere with the measurement of PDPN severity is allowed. 11. Participants who meet any of the following regarding concomitant treatments: 1. Unwilling or unable to discontinue episodic or periodic treatments for pain in the distal legs and/or feet (e.g., injections of local anesthetics). 2. Starting a new non-pharmacological pain treatment (e.g. relaxation/hypnosis, physical or occupational therapy, any exercise-based therapy, any talk-based therapy, acupuncture, TENS) for the treatment of PDPN within 4 weeks prior to screening OR planning on starting a new non-pharmacologic treatment for PDPN OR planned changes to a stable non-pharmacologic treatment for PDPN during the study. i. Non-pharmacological treatment for conditions other than PDPN is allowed without restriction. 12. Active use of opioids or marijuana for any reason at screening and unwilling or unable to discontinue use. 3.2.3. Medical Exclusion Criteria 13. Clinically significant ECG or laboratory abnormalities at the Screening Visit that would put the participant at undue risk or affect the ability of the participant to participate in the trial (in the opinion of the investigator). Screening ECG and lab results may be repeated without requiring a rescreen, as long as the participant is still within the screening window. 14. Participants whose glycemic control has been unstable within 3 months before screening (e.g. ketoacidosis requiring hospitalization). 15. Proliferative retinopathy or maculopathy requiring acute treatment. 16. Requiring dialysis. 17. Myocardial infarction or stroke in the past 6 months. 18. Known diagnosis of moderate to severe hepatic impairment (equivalent to Child-Pugh class B or C) OR aspartate aminotransferase or alanine aminotransferase ≥ 3 times the upper limit of normal during the screening process. 19. A clinically significant illness or operative procedure within 4 weeks of screening. 20. Clinically significant surgery planned during the study period. If a surgery is planned, please contact the MM for approval before randomization. 21. History of malignancy or other medical condition that would put the participant at undue risk or affect the ability of the participant to participate in the trial (in the opinion of the investigator). 22. Pregnant or nursing. 3.2.4. Psychosocial and Substance Use Disorders Exclusion Criteria 23. A clinically significant psychiatric disease that would put the participant at undue risk or affect the ability of the participant to participate in the trial (in the opinion of the investigator). 24. Alcohol use disorder or other substance use disorders (other than nicotine or caffeine) in accordance with DSM-5 criteria within 12 months of screening. 25. Positive urine drug tests defined as one or more of the following (see Urine Drug Testing Section 6.2.13.5.1): 1. Two positive urine drug tests for a prescribed opioid (buprenorphine, opiates, methadone and/or oxycodone), prior to the initiation of investigational product (IP); 2. Two positive urine drug tests for marijuana (prescribed or recreational), prior to the initiation of investigational product (IP); 3. One positive urine drug test for cocaine, ecstasy, methamphetamines, or phencyclidine (PCP); 4. One positive urine drug test for non-prescribed amphetamines, barbiturates, benzodiazepines, or opioids (buprenorphine, opiates, methadone and/or oxycodone). 26. Vulnerable persons defined as either of the following: 1. Individuals whose willingness to volunteer in a clinical study may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Individuals whose judgment has been impaired by their physical, mental, or socio-economical condition and those incapable of giving informed consent.

## Conditions & Interventions

**Interventions:**
DRUG: ISA specific
**Conditions:**
Painful Diabetic Neuropathy

## More Information

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**Principal Investigator:**
**Phase:** PHASE2
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