

# Pharmacokinetic - pharmacodynamic study of amifampridine modified release in LEMS patients

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The aim of this study is to investigate the pharmacokinetics of the extended release formulation of amifampridine. Secondary objective of the study is to develop a PKPD model of amifampridine in LEMS.

<b>Ethical review</b>	Approved WMO
<b>Status</b>	Pending
<b>Health condition type</b>	Neuromuscular disorders
<b>Study type</b>	Observational invasive

## Summary

### ID

NL-OMON56948

### Source

ToetsingOnline

### Brief title

PKPD of amifampridine MR in LEMS patients

### Condition

- Neuromuscular disorders

### Synonym

Lambert-Eaton Myasthenic Syndrome, LEMS

### Research involving

Human

### Sponsors and support

**Primary sponsor:** Leids Universitair Medisch Centrum

**Source(s) of monetary or material Support:** Subsidie vanuit ministerie van VWS aan het Nationaal Farmaceutisch KennisCentrum (NFKC)

## Intervention

**Keyword:** Amifampridine, LEMS, Modified release, PKPD

## Outcome measures

### Primary outcome

Pharmacokinetic parameters: Tmax, Cmax, AUC, VD, Ctough,SS.

### Secondary outcome

Pharmacodynamic endpoints: 3TUG scores, subject global impression (SGI) and CMAP amplitude. The occurrence of side effects will also be assessed.

## Study description

### Background summary

Lambert-Eaton myasthenic syndrome (LEMS) is a very rare antibody-mediated autoimmune disease of the neuromuscular junction. LEMS is characterized by muscle fatigability with weakness in the limb girdle region as most important complaint. Therapy can be divided in symptomatic treatment and immunosuppressive treatment. Symptomatic treatment with amifampridine is the only therapy currently authorized for use in LEMS patients. In the Netherlands the first choice drug is amifampridine base in an extended release formulation, instead of the currently authorized amifampridine phosphate in an immediate release formulation. Although amifampridine base has not received formal authorisation, its use is condoned by regulating authorities based on the extensive (>40 year) experience with this drug, its lower costs and possibly better safety profile due to its extended release properties. However, the extended release properties of the formulation have been shown solely in in vitro dissolution experiments, no in vivo pharmacokinetic parameters have been collected.

### Study objective

The aim of this study is to investigate the pharmacokinetics of the extended release formulation of amifampridine. Secondary objective of the study is to develop a PKPD model of amifampridine in LEMS.

### Study design

A multiple dose open label study.

### **Study burden and risks**

There is extensive experience with the use of amifampridine in patients with LEMS and the dose used in this study is based on the patients clinical response and side effects. Therefore the risk of serious (unexpected) side effects is minimal.

There is no medicinal product started in this study. The intervention entails extra measurements. Additional blood is collected and some pharmacodynamic endpoints are measured more frequent than in common clinical practice, the risk of these additional measurements is minimal. Additional risk may be the delay of the first daily dose of amifampridine because patients will travel to the research center withholding their first daily dose. The risk might be a minimal increase in symptoms of LEMS. A long travel time will increase this risk and an overnight stay near the research center will be offered to reduce this risk.

Benefits are more insight in the pharmacokinetics of amifampridine modified release and with this insight more optimal dosing regimes can be prescribed.

## **Contacts**

### **Public**

Leids Universitair Medisch Centrum

Albinusdreef 2  
Leiden 2300RC  
NL

### **Scientific**

Leids Universitair Medisch Centrum

Albinusdreef 2  
Leiden 2300RC  
NL

## **Trial sites**

### **Listed location countries**

Netherlands

## Eligibility criteria

### Age

Adults (18-64 years)

Elderly (65 years and older)

### Inclusion criteria

1. Age >18 years
2. Clinical diagnosis of LEMS
3. Presence of Voltage Gated Calcium Channel Antibodies (VGCC antibodies)
4. Current use of amifampridine modified release
5. Receiving a stable dose of amifampridine modified release

### Exclusion criteria

1. The patient is unable to fill out the study questionnaires or be interviewed in Dutch or English, or is unable to undergo the tests needed for the study, or is unable to give informed consent for participation in the study.
2. The investigator can exclude patients for this trial which are deemed not suitable for any reason.

## Study design

### Design

**Study type:** Observational invasive

Masking: Open (masking not used)

Control: Uncontrolled

Primary purpose: Treatment

### Recruitment

NL

Recruitment status: Pending

Start date (anticipated): 01-03-2024

Enrollment: 18

Type: Anticipated

## Ethics review

Approved WMO

Date: 14-08-2024

Application type: First submission

Review commission: METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

## Study registrations

### Followed up by the following (possibly more current) registration

No registrations found.

### Other (possibly less up-to-date) registrations in this register

No registrations found.

### In other registers

Register	ID
CCMO	NL85775.058.24