

# Observational Study Description H6D-MC-LVHQ(b) A Prospective Case-Crossover Study to Evaluate the Possible Association Between the Use of PDE5 inhibitors and the Risk of Acute Nonarteritic Anterior Ischaemic Optic Neuropathy (NAION)

**First published:** 13/04/2017

**Last updated:** 30/03/2024

Study

Finalised

## Administrative details

### **PURI**

<https://redirect.ema.europa.eu/resource/18651>

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### **EU PAS number**

EUPAS13266

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### **Study ID**

18651

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## **DARWIN EU® study**

No

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### **Study countries**

United States

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### **Study description**

This is an observational multicentre, case-crossover study design to evaluate the possible association between PDE5 inhibitor exposure and the risk of acute NAION in adult males. All subjects included in the analysis populations had adjudication-confirmed NAION and intermittent PDE5 inhibitor use. A subject was considered an exposed case if their exposure occurred in the predefined time period immediately preceding NAION symptom onset (hazard period). The remaining time was the control period, that time in which exposure occurred without subsequent NAION onset. The exposure window was defined as 5 times the half-life of the PDE5 inhibitor (4 days for tadalafil and 1 day for sildenafil and vardenafil). In the primary analysis, the person-time method was used to calculate a Mantel Haenszel rate ratio for the risk of NAION, comparing PDE5 inhibitor exposure in the 30 days before NAION onset by exposed case definition (ie, exposure within the hazard period). Secondary analyses conducted as part of this study evaluated the Mantel Haenszel rate ratio for person-time for NAION comparing PDE5 inhibitor exposure in the 12 months before NAION onset by exposed case definition. A matched interval analysis method was also conducted assessing PDE5 inhibitor exposure occurring in the hazard periods and matched control periods during the 42 days prior to the acute NAION onset. The study did not examine the risk of NAION in association with any particular PDE5 inhibitor individually, therefore results can be considered applicable to the class.

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### **Study status**

Finalised

## **Research institutions and networks**

# Institutions

## Syneos Health

United Kingdom

**First published:** 23/04/2015

**Last updated:** 06/03/2024

**Institution**

**Non-Pharmaceutical company**

**ENCePP partner**

## Contact details

### Study institution contact

Eva Flahavan

**Study contact**

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### Primary lead investigator

Eva Flahavan

**Primary lead investigator**

## Study timelines

### Date when funding contract was signed

Actual: 02/12/2009

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### Study start date

Planned: 19/04/2010

Actual: 05/05/2010

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### **Date of final study report**

Planned: 18/05/2016

Actual: 26/05/2016

## Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

Eli Lilly and Company

## Regulatory

### **Was the study required by a regulatory body?**

Yes

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### **Is the study required by a Risk Management Plan (RMP)?**

EU RMP category 3 (required)

## Other study registration identification numbers and links

<https://clinicaltrials.gov/show/NCT01131104>

## Methodological aspects

### Study type

### Study type list

**Study topic:**

Disease /health condition  
Human medicinal product

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**Study type:**

Non-interventional study

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**Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

**Data collection methods:**

Primary data collection

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**Main study objective:**

The objective of this noninterventional, case-crossover, observational study was to evaluate whether there is a possible association between exposure to PDE5 inhibitors and the risk of acute NAION in adult males.

## Study Design

**Non-interventional study design**

Other

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**Non-interventional study design, other**

Case-crossover

## Study drug and medical condition

**Name of medicine**

CIALIS

LEVITRA

VIAGRA

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**Medical condition to be studied**

Optic ischaemic neuropathy

Optic neuropathy

Optic neuritis

## Population studied

**Short description of the study population**

Adult subjects from US who experienced abrupt visual loss (defined as visual loss typically occurring during less than a 1-day period or visual loss noted upon awakening) in one eye and presented to an ophthalmologist within 45 days of onset of NAION symptoms for an initial visit that resulted in a diagnosis of suspected NAION by the investigator.

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**Age groups**

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

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**Estimated number of subjects**

350

## Study design details

## **Outcomes**

The primary objective of this case-crossover study examined the rate of acute NAION occurring in patients with PDE5 inhibitor exposure in the hazard periods (immediately preceding NAION onset) compared with exposure occurring over the 30 days before NAION onset, expressed as a Mantel Haenszel rate ratio for person-time. Secondary analyses included (1) a person-time analysis evaluating acute NAION occurring in patients with PDE5 inhibitor exposure in the hazard periods compared with exposure over the 12 months prior to NAION onset, and (2) a matched interval analysis method assessing PDE5 inhibitor exposure during hazard periods and matched controlled periods the 42 days prior to NAION onset.

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## **Data analysis plan**

This case-crossover study was conducted to evaluate the possible association between PDE5 inhibitor exposure and the risk of acute NAION in adult males. Exposure was based on the PDE5 inhibitor effect period (5 times the half-life). The primary analysis used the person-time method, including subjects with adjudication-confirmed NAION who had intermittent exposure to PDE5 inhibitors. In this analysis, a Mantel Haenszel rate ratio for the risk of NAION was calculated, comparing PDE5 inhibitor exposure in the 30 days before NAION onset by exposed case definition (ie, exposure within the hazard period). A secondary analysis, using the person-time method examined this risk using PDE5 inhibitor exposure over the 12 months prior to NAION onset. Other secondary analyses, used the matched interval method to evaluate the association between PDE5 inhibitor exposure in the 42 days prior to acute NAION, evaluated using a 4-day hazard period and a series of 4 preceding 4-day control intervals.

## **Documents**

## Study results

[LY450190 H6D-MC-LVHQ PASS full CSR redacted.pdf\(3.79 MB\)](#)

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## Study publications

[Flahavan EM, Li H, Gupte-Singh K, Rizk RT, Ruff DD, Francis JL and Kinchen KS.](#)

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# Data management

## Data sources

### Data sources (types)

[Other](#)

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### Data sources (types), other

Prospective patient-based data collection

## Use of a Common Data Model (CDM)

### CDM mapping

No

## Data quality specifications

### Check conformance

Unknown

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## **Check completeness**

Unknown

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## **Check stability**

Unknown

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## **Check logical consistency**

Unknown

# Data characterisation

## **Data characterisation conducted**

Unknown