

# Post-marketing study of ropinirole prolonged release tablets in Parkinson's disease: Evaluation outcomes associated with long term use of Ropinirole-PR using the clinical practice research datalink (CPRD) (111981)

**First published:** 23/02/2016

**Last updated:** 23/05/2024

Study

Finalised

## Administrative details

### PURI

<https://redirect.ema.europa.eu/resource/40748>

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### EU PAS number

EUPAS12518

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### Study ID

40748

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## **DARWIN EU® study**

No

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### **Study countries**

☐ United Kingdom

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### **Study description**

Parkinson disease (PD) is a neurodegenerative condition resulting in the deficiency of dopamine, current available therapies aim to compensate for its deficiency. Ropinirole is non-ergot DA indicated for the treatment of PD. The immediate release formulation was approved over 15 years ago, a prolonged release formulation (ropinirole-PR) was more recently licensed in 2008. The proposed study is part of a post-marketing commitment to the MHRA to evaluate long term safety of ropinirole-PR. Specifically, it is proposed to estimate the incidence of dyskinesias, on-off phenomena (subject to feasibility) and impulse control disorders, in PD patients initiating ropinirole-PR monotherapy vs. initiators of immediate release DA monotherapy. This retrospective observational study will use longitudinal electronic medical records (EMR) from the UK- Clinical Practice Research Datalink (CPRD) supplemented with GP questionnaire data. Treatment persistence, adherence off-label use of ropinirole-PR will be also be evaluated. A propensity matched cohort design with adjustments for time varying covariates will be used.

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### **Study status**

Finalised

## **Research institutions and networks**

### **Institutions**

# GlaxoSmithKline (GSK)

**First published:** 01/02/2024

**Last updated:** 01/02/2024

Institution

## Contact details

### Study institution contact

GSK Clinical Disclosure Advisor GSK Clinical Disclosure Advisor

Study contact

[Pharma.CDR@gsk.com](mailto:Pharma.CDR@gsk.com)

### Primary lead investigator

GSK Clinical Disclosure Advisor GSK Clinical Disclosure Advisor

Primary lead investigator

## Study timelines

### Date when funding contract was signed

Planned: 29/09/2015

Actual: 29/09/2015

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### Study start date

Planned: 31/03/2016

Actual: 07/04/2016

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

Planned: 26/04/2018

Actual: 30/04/2018

## Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

GlaxoSmithKline

## Study protocol

[gsk-111981-protocol-redact.pdf](#)(1.57 MB)

## 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)

## 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

Drug utilisation

**Data collection methods:**

Secondary use of data

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**Main study objective:**

To estimate, the incidence of dyskinesia in PD patients initiating ropinirole-PR monotherapy vs. immediate release dopamine agonist monotherapy. Other outcomes of interest are on-off phenomena (subject to feasibility) and impulse control disorders.

## Study Design

**Non-interventional study design**

Cohort

## Study drug and medical condition

## **Anatomical Therapeutic Chemical (ATC) code**

(N04BC) Dopamine agonists

Dopamine agonists

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## **Medical condition to be studied**

Parkinson's disease

## **Population studied**

### **Short description of the study population**

The populations of interest comprised of individuals on the CPRD with a recorded Parkinson's disease diagnosis that had initiated either ropinirole-PR monotherapy (ropinirole-PR) or an oral immediate release dopamine agonist (IR-DA) as monotherapy between 2008 and 2013.

Inclusion criteria:

Individuals were required to

- Meet the case definition of Parkinson's disease
- Have initiated a dopamine agonist therapy between 2008-2013 and received at least two prescriptions for the therapy of interest.
- Have a minimum of 12 months of registration prior the date of initiation of the dopamine agonist therapy +30 days in order to collect information on disease, comorbidity, medical and prescription history.
- Belong to practices that are considered up to research standard at initiation of therapy.

Exclusion criteria

- Individuals in the immediate release dopamine agonist cohort that had

previously been prescribed any prolonged release dopamine agonist (ropinirole-PR or pramipexole-PR) were excluded.

- Individuals with evidence of adjunctive or prior history of levodopa use at time of initiating the dopamine agonist therapy were excluded, as were individuals with a history of dyskinesia or impulse control disorders prior to index date.
  - Individuals with evidence of secondary or drug induced PD
  - Aged <40 years at the time of PD diagnosis
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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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### **Special population of interest**

Other

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### **Special population of interest, other**

Parkinson's disease patients

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### **Estimated number of subjects**

2000

## **Study design details**

## Outcomes

Dyskinesia is the primary outcome. Additional outcomes are impulse control behaviors (ICD) and on-off phenomena. Dyskinesia and ICD will be identified using READ codes on the CPRD supplemented by GP questionnaire. On-off phenomena will be identified solely by GP questionnaire, however, it may not be feasible or appropriate to evaluate this as an outcome should the GP response rate be low, Treatment persistence and adherence will be evaluated.

Additionally time to levodopa initiation will be estimated. As levodopa is associated with dyskinesias, delay in its use may further reduce the risk of the development of motor complications, or reflect better control of PD symptoms by current therapy. The extent of off-label use of ropinirole-PR will be described.

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## Data analysis plan

The incidence of dyskinesia (and other outcomes of interest) will be calculated in the ropinirole-PR and propensity score matched IR-DA cohorts. Censoring occurs at the earliest of an outcome of interest, discontinuation of therapy+30days, end of a patient record or end of the study period. Crude incident rates per 1000 person years of follow-up for each outcome will be calculated. Incidence rates will be stratified by age group (at index date) and PD duration. Incidence rate ratios will be estimated between the exposure groups and adjusted for risk factors using multivariable Poisson regression. In addition, the incidence amongst switchers to ropinirole-PR and those initiating ropinirole-PR de novo will be estimated. A Cox proportional hazards regression model will be used to evaluate time to dyskinesias in individuals in both cohorts. Adjusted hazards ratios will be estimated, accounting for potential confounders and time varying covariates.

# Documents

## Study results



## Data management

### Data sources

#### **Data source(s)**

Clinical Practice Research Datalink

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#### **Data sources (types)**

[Electronic healthcare records \(EHR\)](#)

[Other](#)

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#### **Data sources (types), other**

Data from CPRD will be supplemented by GP questionnaire data

### 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**

No