

# Long-Term Post-Marketing Observational Study of the Safety of Roflumilast

**First published:** 22/08/2016

**Last updated:** 02/04/2024

Study

Finalised

## Administrative details

### EU PAS number

EUPAS14852

### Study ID

50538

### DARWIN EU® study

No

### Study countries

☐ Germany

☐ Norway

☐ Sweden

☐ United States

## Study description

Chronic obstructive pulmonary disease (COPD) is a leading cause of death. Takeda Development Centre (Europe) Ltd (formerly Nycomed) received central marketing authorization in the EU in July 2010 and regulatory approval in Canada in November 2010 for its selective phosphodiesterase-4 (PDE4) inhibitor roflumilast (DAXAS®), which is available as 500µg tablets (once daily) for maintenance treatment of severe COPD associated with chronic bronchitis in adults with a history of frequent exacerbations as add on to bronchodilator treatment. Roflumilast is contraindicated in patients with hypersensitivity to the tablet ingredients and in patients with moderate to severe liver impairment. Since roflumilast is used for maintenance treatment, a long-term safety assessment exceeding 12 months was requested as a condition of approval for marketing in the EU. During the approval process, Takeda as the Marketing Authorisation Holder (MAH) for roflumilast, committed to the European Medicines Agency (EMA) to perform a database study, and proposed that the study be conducted in large, unselected COPD populations, reflecting the use of roflumilast in a real-life setting. Established electronic health care databases in countries where roflumilast is on the market and data on a meaningful number of roflumilast treated patients is captured will be the source on which to base this Post-Authorisation Safety Study (PASS). Due to the sponsorship transfer that occurred in 2015, study is now sponsored by AstraZeneca. The study is conducted by independent investigators qualified in epidemiology. The patient data will remain the properties of the respective database owners, and AstraZeneca will not have direct access to the data but will be co-owner of the results derived from these data, together with the respective investigators. The Lead Investigator will lead the team of investigators, each of whom is responsible for the conduct of the study.

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## Study status

Finalised

## Research institutions and networks

## Institutions

### Real World Solutions, IQVIA

☐ Netherlands

☐ United Kingdom (Northern Ireland)

**First published:** 28/04/2011

**Last updated:** 22/03/2024

Institution

Other

ENCePP partner

### Leibniz Institute for Prevention Research and Epidemiology - BIPS

☐ Germany

**First published:** 29/03/2010

**Last updated:** 26/02/2024

Institution

Not-for-profit

ENCePP partner

### Epi Research Oy Finland, Quintiles Real World and Late Phase Research (RWLPR), EMR Data and Analytics USA

## Contact details

**Study institution contact**

Edeltraut Garbe ClinicalTrialTransparency@astrazeneca.com

Study contact

ClinicalTrialTransparency@astrazeneca.com

**Primary lead investigator**

Edeltraut Garbe

Primary lead investigator

## Study timelines

**Date when funding contract was signed**

Actual: 01/07/2010

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**Study start date**

Planned: 13/10/2013

Actual: 30/03/2013

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**Data analysis start date**

Planned: 31/01/2020

Actual: 30/03/2013

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**Date of interim report, if expected**

Planned: 31/10/2017

Actual: 31/10/2017

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**Date of final study report**

Planned: 31/12/2022

Actual: 16/12/2022

## Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

AstraZeneca

## Study protocol

[RO-2455-403-RD\\_ProtocolVersion2.4-31Jul13.pdf](#)(285.69 KB)

[D7120R00003\\_ProtocolVersion3\\_updated20170207.pdf](#)(443.37 KB)

## 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 1 (imposed as condition of marketing authorisation)

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### **Regulatory procedure number**

D7120R00003

## Other study registration identification numbers and links

D7120R00003

## Methodological aspects

**Study topic:**

Disease /health condition

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**Study type:**

Non-interventional study

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**Scope of the study:**

Safety study (incl. comparative)

**Data collection methods:**

Secondary use of data

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**Main study objective:**

The objective of this study is to evaluate the long-term safety of roflumilast in the treatment of COPD, with focus primarily on all-cause mortality.

## Study Design

**Non-interventional study design**

Cohort

Other

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**Non-interventional study design, other**

Observational study

## Study drug and medical condition

**Medical condition to be studied**

Chronic obstructive pulmonary disease

## Population studied

## Short description of the study population

The study population comprised of patients aged 40 years or older diagnosed with chronic obstructive pulmonary disease (COPD) exposed or unexposed to the treatment of roflumilast identified through the databases in Germany, Sweden, the United States, and Norway.

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### Age groups

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

Patients with chronic obstructive pulmonary disease

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### Estimated number of subjects

21812

## Study design details

### Outcomes

The primary outcome for this study is all-cause 5 year mortality, Death by suicide or hospitalization due to suicide attempt, hospitalization for any cause, major cardiovascular events leading to hospitalization, hospitalization related to respiratory disease, new diagnosis of depression, new diagnosis of cancer, hospitalization due to diarrhea of non-infectious origin, abnormal unexplained

weight loss, new diagnosis of tuberculosis or hepatitis B or C.

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### **Data analysis plan**

The primary outcome (5-year all cause mortality) will be evaluated by a Cox proportional hazards regression model for counting processes, which allow the follow-up time to be divided into several periods and therefore control for baseline and time-dependent covariates, using the full observational period of available data, i.e. up to 9 years of follow up. The Cox proportional hazards regression will take into account the fact that individual matching was performed (based on age, sex and propensity score) by considering the exposed patient and his/her matched controls as one stratum and including this as a stratum in the Cox proportional hazards model. Additional variables will be included in the model if available.

## **Documents**

### **Study results**

[DAXAS Final Study Report\\_Redacted\\_Reduced.pdf](#)(1.85 MB)

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### **Study report**

[DAXAS Final Study Report Addendum \(NOR\)\\_Redacted.pdf](#)(8.6 MB)

## **Data management**

### **ENCePP Seal**

The use of the ENCePP Seal has been discontinued since February 2025.

The ENCePP Seal fields are retained in the display mode for transparency



but are no longer maintained.

## Data sources

### Data source(s)

Sweden National Prescribed Drugs Register / Läkemedelsregistret

German Pharmacoepidemiological Research Database

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### Data sources (types)

[Administrative healthcare records \(e.g., claims\)](#)

[Disease registry](#)

[Drug dispensing/prescription data](#)

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

[Other](#)

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### Data sources (types), other

Discharge registry, death registry, cancer registry, and registries holding socio-demographic 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