# Impact of EU label changes and revised pregnancy prevention programme for oral retinoid containing medicinal products: utilization and prescribing trends

**First published:** 19/09/2019
**Last updated:** 23/05/2024

Study | Finalised

## Administrative details

**PURI**
https://redirect.ema.europa.eu/resource/49667

**EU PAS number**
EUPAS31095

**Study ID**
49667

**DARWIN EU® study**
No

**Study countries**
Denmark
France
Italy
Netherlands
Spain

**Study description**
Oral retinoids are used to treat dermatological conditions like severe acne vulgaris (isotretinoin) psoriasis (acitretin) and chronic hand eczema (alitretinoin), some oral retinoids are also used to treat skin manifestations of T-cell lymphoma (bexarotene) and acute

promyelocytic leukaemia (tretinoin). All oral retinoids are highly teratogenic and must not be used during pregnancy. The aim of this study is to investigate the use of oral retinoid containing medicinal products authorised in the EU before and after implementation of the 2018 revised measures for pregnancy prevention in clinical practice.

**Study status**
Finalised

# Research institution and networks

## Institutions

### University Medical Center Utrecht (UMCU)

Netherlands
**First published:** 24/11/2021
Last updated 22/02/2024

Institution
Hospital/Clinic/Other health care facility
Educational Institution
ENCePP partner

### The PHARMO Institute for Drug Outcomes Research (PHARMO Institute)

Netherlands
**First published:** 07/01/2022
Last updated 10/01/2022

Institution
ENCePP partner
Laboratory/Research/Testing facility

### Danish National Registries Denmark, BIFAP Spain, FISABIO Valencia, Spain, Caserta Camania, Italy, Palermo Sicily, Italy, SNIRAM France

## Networks

# EU Pharmacoepidemiology and Pharmacovigilance (PE&PV) Research Network

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

## Contact details


**Study institution contact**
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**Primary lead investigator**
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Primary lead investigator


## Study timelines

**Date when funding contract was signed**
Planned:
25/02/2019
Actual:
25/02/2019

**Study start date**
Planned:
01/01/2010
Actual:
01/01/2010

**Data analysis start date**
Planned:
01/08/2020

**Date of final study report**
Planned:
25/12/2021

Actual:
31/10/2022

## Sources of funding

- EMA

## Study protocol

Protocol Retinoids V0.5 19SEP2019.pdf(1.71 MB)

AMEND Protocol Retinoids V1.2 17DEC2021.pdf(1.34 MB)

## Regulatory

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

**Is the study required by a Risk Management Plan (RMP)?**
Not applicable

# Methodological aspects

## Study type

## Study type list

**Study topic:**
Human medicinal product

**Study type:**
Non-interventional study

**Scope of the study:**
Assessment of risk minimisation measure implementation or effectiveness
Drug utilisation

**Data collection methods:**
Secondary data collection

**Main study objective:**
This study will address the research question, "What was the effect of the EU label changes and the revised pregnancy prevention programme (2018) on utilization of oral retinoids and to what extent did prescribers and patients comply with recommendations?".

# Study Design

**Non-interventional study design**
Cohort

# Study drug and medical condition

**Anatomical Therapeutic Chemical (ATC) code**
(D05BB02) acitretin
(D10BA01) isotretinoin
(D11AH04) alitretinoin

# Population studied

**Short description of the study population**
Female subjects of childbearing potential aged 12-55 years using oral retinoid containing medicinal products identified from the data sources of Netherlands, Denmark, Italy and Spain between 01 January 2010 and 31 December 2020.

**Age groups**
Adolescents (12 to < 18 years)
Adults (18 to < 46 years)
Adults (46 to < 65 years)

**Special population of interest**
Pregnant women

**Estimated number of subjects**
9000000

# Study design details

**Outcomes**
- retinoid use (dispensing/prescription) (objective 1) - pregnancy test (objective 2) - contraceptive use (objective 2) - pregnancy (objective 3) - use of alternative medicines (objective 4), - reason for discontinuation of retinoids (objective 1)

**Data analysis plan**
1. Descriptive and hypothesis testing (objectives 1 through 4) - Incidence rates and quarter-year prevalences of outcomes will be calculated. - Interrupted time series analysis will be performed to test changes in outcomes before vs. after implementation of PRAC intervention. 2. Overall evaluation (objective 5) - The results of objectives 1-4 will be summarized qualitatively.

## Documents

**Study results**
Finalreports_retinoids_v2.1_SUMMARY.pdf(174.63 KB)

**Study publications**
Durán CE, Riera-Arnau J, Abtahi S, Pajouheshnia R, Hoxhaj V, Gamba M, Alsina E,… Sturkenboom, Miriam, Klungel, Olaf, Durán, Carlos E., Riera-Arnau, Judit, Abtah…

# Data management

## ENCePP Seal

**This study has been awarded the ENCePP seal**


**Conflicts of interest of investigators**
empty_file_1.pdf(11.35 KB)

**Composition of steering group and observers**
Information DoI and steering group EUPAS31095.pdf(140.4 KB)

**Signed code of conduct**
Declaration of Compliance with the ENCEPP Code of Conduct.pdf(71.22 KB)

**Signed code of conduct checklist**

Checklist for the ENCEPP Code of Conduct.pdf(390.09 KB)

**Signed checklist for study protocols**
ENCEPP Checklist for Study Protocols.pdf(402.38 KB)

# Data sources

**Data source(s)**
Danish registries (access/analysis)
Caserta claims database
PHARMO Data Network
Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público (Pharmacoepidemiological Research Database for Public Health Systems)
ARS Toscana

**Data source(s), other**
Danish Registries (access/analysis), Caserta database, PHARMO Data Network, BIFAP, ARS, FISABIO

**Data sources (types)**
Administrative data (e.g. claims)
Disease registry
Drug dispensing/prescription data
Electronic healthcare records (EHR)

# Use of a Common Data Model (CDM)

**CDM mapping**
No

# Data quality specifications

**Check conformance**
Unknown

**Check completeness**
Unknown

**Check stability**
Unknown

**Check logical consistency**
Unknown

# Data characterisation

**Data characterisation conducted**
No