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: 04/12/2025

Study Finalised

Administrative details

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 institutions and networks

Institutions

University Medical Center Utrecht (UMCU)

Netherlands

First published: 24/11/2021

Last updated: 22/02/2024

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

Health Services Research and Pharmacoepidemiology Unit (HSRP Unit) FISABIO

Spain

First published: 30/11/2023

Last updated: 30/11/2023

Institution | Other | ENCePP partner

The PHARMO Institute for Drug Outcomes Research (PHARMO Institute)

Netherlands

First published: 07/01/2022

Last updated: 19/12/2025

Institution | Non-Pharmaceutical company | ENCePP partner

Agencia Española de Medicamentos y Productos Sanitarios (Spanish Agency for Medicines and Medical Devices, AEMPS)

Spain

First published: 01/02/2024

Last updated: 04/09/2024

Institution | EU Institution/Body/Agency | Not-for-profit | Regulatory Authority | ENCePP partner

Danish National Registries Denmark, Caserta Camania, Italy, Palermo Sicily, Italy, SNIRAM France

Networks

EU Pharmacoepidemiology and Pharmacovigilance (PE&PV) Research Network

☐ Netherlands

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Network

Contact details

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Study contact

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Primary lead investigator

Miriam Sturkenboom

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 use of data

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

acitretin

(D10BA01) isotretinoin

isotretinoin

(D11AH04) alitretinoin

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

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.

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

BIFAP - 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 healthcare records (e.g., claims)

Disease registry

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