DARWIN EU® - Characterisation of exposure to acitretin and purpura and related conditions

First published: 04/01/2025

Last updated: 07/08/2026

Study Ongoing

Administrative details

EU PAS number

EUPAS1000000429

Study ID

1000000429

DARWIN EU® study

Yes

Study countries

- Denmark
- Netherlands
- Spain
- United Kingdom

Study description

The Marketing Authorisation Holders (MAHs) that hold Marketing Authorisations (MAs) for acitretin in Canada and the US have included purpura in their label. The Pharmacovigilance Risk Assessment Committee (PRAC) requested additional real-world evidence (RWE) to assess the causal association between certain purpura and related conditions and acitretin before deciding whether to include selected purpura and related conditions in section 4.4 (or 4.8) of the Summary of product characteristics (SmPC) of acitretin.

Acitretin (D05BB02) is a synthetic aromatic analogue of retinoic acid. Retinol (a derivative of Vitamin A) is known to be essential for normal epithelial growth and differentiation. Acitretin is a Nationally Authorised Product (NAP) with approved indications including severe forms of psoriasis (erythrodermic psoriasis and local or generalized pustular psoriasis); severe disorders of keratinization such as congenital ichthyosis, pityriasis rubra pilaris, and Darier's disease. And other disorders of keratinization which may be resistant to other therapies. It is authorised in the majority of EU countries (not in Bulgaria, Cyprus, Greece, Malta, Romania).

This study aims to characterise patients treated with acitretin, estimate the incidence rate of purpura and related conditions in patients with treatment indications for acitretin.

Study status

Ongoing

Research institutions and networks

Institutions

Department of Medical Informatics - Health Data Science, Erasmus Medical Center (ErasmusMC)

Netherlands

First published: 03/11/2022

Last updated: 02/05/2024

Institution | Educational Institution | ENCePP partner

Networks

Data Analysis and Real World Interrogation Network (DARWIN EU®)

- Belgium
- Croatia
- Denmark
- Estonia
- Finland
- France
- Germany
- Greece
- Hungary
- Italy
- Lithuania
- Netherlands
- Norway

Poland
Portugal
Spain
Sweden
United Kingdom
United States

First published: 01/02/2024

Last updated: 05/11/2026

Network

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Cheryl Tan

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 31/07/2024

Actual: 31/07/2024

Study start date
Planned: 12/12/2024

Actual: 12/12/2024

Date of final study report
Planned: 30/04/2025

Sources of funding

- EMA

Study protocol

DARWIN EU_Protocol_P3-C1-021_Acitretin and purpura_V2.pdf (921.97 KB)

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:

Drug utilisation

Data collection methods:

Secondary use of data

Study design:

• New drug user cohort (Objectives 1-2)

• Population-level descriptive epidemiology (Objective 3)

Main study objective:

1. To characterise patients initiating treatment of acitretin in terms of:

a. Demographics

b. Treatment indications

c. Risk factors for purpura and related conditions

d. Comorbidities

2. To describe patient-level acitretin utilisation in a cohort of new users including:

a. Duration of treatment

b. Concomitant medications prescribed at/before/after index date

3. To estimate crude and age-sex standardised incidence rates of purpura and related conditions (and stratified by thrombocytopenic purpura vs non-

thrombocytopenic purpura) in patients with common indications for acitretin and/or treatment groups, namely:
a. Treatment: methotrexate, cyclosporine, azathioprine-containing immunosuppressants; acitretin; TNF alpha inhibitors; interleukin inhibitors
b. Indication (psoriasis vs other)
c. Treatment-indication combination: Acitretin-psoriasis, Acitretin-keratinization, Acitretin-unknown/other, Methotrexate-psoriasis, Azathioprine/cyclosporine immunosuppressants-psoriasis, TNF alpha inhibitors-psoriasis, Interleukin inhibitors-psoriasis

Study Design

Non-interventional study design
Cohort

Study drug and medical condition

Study drug International non-proprietary name (INN) or common name
ACITRETIN

Anatomical Therapeutic Chemical (ATC) code
(D05BB02) acitretin
acitretin

Medical condition to be studied
Purpura

Population studied

Short description of the study population

Patient-level characterisations (Objectives 1-2): New users of acitretin in the study period between 01/01/2010 and 31/12/2023 (or the latest date of data availability of the respective databases), with at least 365 days of visibility prior to the date of their first prescription and no prior use of acitretin.
Population-level descriptive epidemiology (Objective 3): New users of acitretin, alternative treatments, and/or diagnosis of a condition of interest in the study period between 01/01/2010 and 31/12/2023 (or the latest date of data availability of the respective databases), with at least 365 days of visibility prior to the date of their first prescription and no prior use of the respective drug/s, will comprise the denominator population based on the respective treatment and indication groups.

Study design details

Outcomes

Outcomes of interest for the new-user cohort study were purpura and related conditions.

Data analysis plan

Statistical analysis
Analytical methods:
Patient level characterisation was conducted any time before or on index date (date of first prescription of acitretin), including patient demographics, treatment indications, comorbidities pre-specified as known risk factors for purpura and related conditions. For drug utilisation, duration of treatment and concomitant medications at index date, 90 days before and 90 days after index date was reported.

Incidence rates (IRs) were calculated for purpura and related conditions in acitretin users, those of other major treatment groups and those indicated for treatment with acitretin. Incidence rates per 100,000 person years were estimated crude and age-sex standardised using the European Standard Population. Results were reported for overall purpura and related conditions, and for thrombocytopenic purpura vs non-thrombocytopenic purpura.
For all analyses a minimum cell counts of 5 was used when reporting results, with any smaller counts noted
as <5.

Summary results

Broadly, our study aimed to characterise acitretin use and purpura and related conditions across four routinely collected healthcare databases in the UK, Netherlands, Spain, and Denmark. New users of acitretin were generally in their mid-50s to 60s and with a higher proportion of males compared to females. Psoriasis was the most common indication, and the most common risk factor of acitretin new use was infectious disease. Across the four databases, the median number of acitretin prescriptions ranged between 1 and 2, and treatment duration ranged from 30 to 159 days. Most frequent comedications were systemic antibacterials, antidepressants and anti-inflammatory/anti-rheumatic drugs.
Due to low number of events of purpura and related conditions overall in IPCI, IRs were not calculated for this database. Among the other three databases, age-sex standardised IRs for purpura and related conditions showed that events were uncommon (<1/100 to > 1/1000) to very rare (<1/10 000). Non-thrombocytopenic purpura showed consistently higher standardised rates than thrombocytopenic purpura.
The psoriasis treatment group had the highest number of events. In this treatment group, the outcome of overall purpura and related conditions were uncommon in CPRD GOLD and rare (<1/1000 to ≥ 1/10 000) in SIDIAP and DK-

DHR. Moreover, the outcome of non-thrombocytopenic purpura among patients with psoriasis was rare for all three databases and thrombocytopenic purpura was very rare. Across all databases, the treatment group of acitretin did not have enough outcomes for IRs to be calculated.
Taken together, our results suggest that acitretin is most commonly used for psoriasis, and the outcome of purpura was rare in our populations of interest.

Documents

Study report

DARWIN EU_Report_P3-C1-021 Acitretin and Purpura_V3.pdf (1.09 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)

The Information System for Research in Primary Care (SIDIAP)

Integrated Primary Care Information (IPCI)

Danish Health Data Registries

Clinical Practice Research Datalink (CPRD) GOLD

Use of a Common Data Model (CDM)

CDM mapping

Yes

CDM Mappings

CDM name

OMOP

CDM website

https://www.ohdsi.org/Data-standardization/

CDM version

https://ohdsi.github.io/CommonDataModel/index.html

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

Unknown