Isotretinoin, Contraception, and Pregnancy Outcomes

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Study Ongoing

Administrative details

EU PAS number

EUPAS1000000927

Study ID

1000000927

DARWIN EU® study

No

Study countries

☐ Canada

Study description

Isotretinoin is commonly used in the treatment of severe acne. However, it is known to cause birth defects. To minimize this risk, the pregnancy prevention program in Canada requires the simultaneous use of two methods of

contraception during isotretinoin therapy, among other safeguards. Findings from our previous study suggest suboptimal adherence to, or implementation of, the pregnancy prevention program. The main objective is to update our previous study to examine the frequency and change in frequency over time of contraception use, pregnancy occurrence, and pregnancy outcomes in individuals of childbearing age prescribed isotretinoin from 1997 to present. We will conduct a retrospective cohort study using administrative health care data from 5 Canadian provinces. We will identify female patients aged between 12 and 48 years old, inclusive, who initiated treatment with isotretinoin between 1997 and 2023. Patient and prescriber characteristics at treatment initiation will be described. We will estimate the utilization of contraception before, during, and after isotretinoin therapy. Pregnancy occurrence during and shortly after isotretinoin therapy will be estimated. We will examine trends over time to assess changes in contraception use and pregnancy incidence annually. Among pregnancies exposed to isotretinoin, we will identify the occurrence of pregnancy outcomes (live birth, spontaneous abortion, induced abortion, stillbirth, and termination for fetal anomaly). Rates of congenital malformations among live births following isotretinoin exposure will also be estimated.

Study status

Ongoing

Research institutions and networks

Institutions

Lady Davis Institute

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Institution

University of British Columbia

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Institution

University of Calgary, Calgary, Canada

University of Manitoba, Winnipeg, Canada

ICES, Toronto, Canada

Saskatchewan Health Quality Council, Saskatoon, Canada

Networks

Canadian Network for Observational Drug Effect Studies (CNODES)

Contact details

Study institution contact

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Primary lead investigator

Colin Dormuth

Primary lead investigator

Study timelines

Date when funding contract was signed
Actual: 23/10/2025

Study start date
Actual: 23/10/2025

Date of final study report
Planned: 23/03/2027

Sources of funding

- Other

More details on funding

CNODES is a collaborating core network partner of CoLab, which is funded for query-related activity by Canada’s Drug Agency (CDA, grant number C222 360).

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

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Study design:

Multicentre retrospective cohort study

Main study objective:

1) To estimate the frequency and change in frequency over time of contraception use in individuals of childbearing age prescribed isotretinoin from 1997 to present.
2) To examine the frequency and change in frequency over time of pregnancy and pregnancy outcomes in individuals of childbearing age prescribed isotretinoin from 1997 to present including:
a. Pregnancies overlapping isotretinoin exposure and quantification of the extent of overlap by trimester
b. Pregnancies with isotretinoin exposure that reached live birth with and without congenital abnormalities
c. Pregnancies with isotretinoin exposure that ended with induced abortion, spontaneous abortion, or stillbirth
3) Describe prescriber specialty (e.g., family physician, dermatologist) of the health professionals who prescribe isotretinoin.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

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

ISOTRETINOIN

Anatomical Therapeutic Chemical (ATC) code

(D10BA01) isotretinoin

isotretinoin

Medical condition to be studied

Pregnancy

Stillbirth

Abortion spontaneous

Abortion induced

Live birth

Additional medical condition(s)

Termination of pregnancy for fetal anomaly; Congenital malformations

Population studied

Short description of the study population

The study population will include female patients aged between 12 and 48 years old (18 years and older in Alberta) who initiated treatment with isotretinoin between 1997 and 2023.

Age groups

- Adolescents (12 to < 18 years)
- Adults (18 to < 65 years)
    - Adults (18 to < 46 years)
    - Adults (46 to < 65 years)

Special population of interest

Pregnant women

Women of childbearing potential not using contraception

Women of childbearing potential using contraception

Study design details

Setting

We will use administrative health care data from 5 Canadian provinces (Alberta, British Columbia, Manitoba, Ontario, and Saskatchewan). In each province, the source population will include all female residents who registered for provincial medical services coverage between January 1, 1996, and December 31, 2024. From the source population, we will identify female patients aged between 12 and 48 years old, inclusive, who initiated treatment with isotretinoin between January 1, 1997 (or one year after the earliest data of data availability in each province) and December 31, 2023 (the latest accrual date that will allow adequate follow-up time for outcome ascertainment). The date of the first dispensing will be the cohort entry date. We will exclude patients who received a prescription for isotretinoin in the previous 365 days and those with less than 12 months of health plan enrollment. Patients will be allowed to enter the cohort multiple time provided they meet the eligibility criteria.

For each pregnancy identified among isotretinoin users, we will estimate the pregnancy start date (estimated last menstrual period) and the pregnancy end date (date of outcome, described subsequently) using a validated algorithm (Dormuth, 2021). We will then assess the estimated pregnancy period overlap (by trimester) with isotretinoin treatment duration. An isotretinoin exposure will be considered to overlap with a pregnancy if any day of the isotretinoin episodes (including the days supply and a pre-specified grace period) falls within the estimated gestation period. Preconception exposure will be defined as isotretinoin exposure that occurred within 30 days prior to the estimated last menstrual period. For pregnancies ending in live birth, we will follow infants for 365 days to capture congenital malformations.

Comparators

Not applicable

Outcomes

We will study the following outcomes:

1) Occurrence of seven pregnancy outcomes, where the duration of isotretinoin treatment overlaps with estimated gestational period. These will include: a composite pregnancy outcome, stillbirth subset (includes birth type mixed subset), spontaneous abortion subset, induced abortion subset, live birth only subset, termination of pregnancy for fetal anomaly only subset, and congenital malformations.

2) Overall utilization of contraceptives before, during, and after treatment with isotretinoin. Contraceptives will include (when feasible with the available data): contraceptive pills, intrauterine devices (IUDs) – hormonal and copper, hormonal implant, hormonal vaginal ring, hormonal patch, and contraceptive injection.

3) Overall utilization of other anti-acne medications (systemic antibiotics, topical antibiotics, topical retinoids, and miscellaneous agents) before, during, and after treatment [AS6.1][AS6.2]with isotretinoin.

Data analysis plan

Analyses will be completed in each provincial database with results combined where appropriate. We will describe patient demographics, prescribing characteristics, and other medication use at treatment initiation. We will estimate the utilization of contraception use before, during, and after therapy, expressed as the number of users per 100 isotretinoin episodes, overall, by age category, and by calendar year. We will estimate pregnancy incidence during and shortly after isotretinoin therapy. Among pregnancies with overlap, we will summarize the timing of exposure (i.e., duration of overlap by trimester and evidence of contraception use). We will quantify preconception exposure as well as pregnancies by age category. We will also examine trends over time to assess changes in contraception use and pregnancy incidence annually. Secondary analyses will further explore pregnancy outcomes (described

previously) per 1,000 users, patterns of contraceptive use, isotretinoin prescriber patterns, and repeat isotretinoin episodes.

Documents

Link to project page on CNODES website.

Pregnancy dating algorithm

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), other

Provincial administrative health databases

Data sources (types)

Administrative healthcare records (e.g., claims)

Pharmacy dispensing records

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

Unknown