

# Safety of IL-17 and IL-23 inhibitors as treatment for immune mediated inflammatory diseases at conception and during pregnancy: an ENTIS study. (SAFE-PPREG)

**First published:** 26/03/2026

**Last updated:** 26/03/2026

Study

Ongoing

## Administrative details

### EU PAS number

EUPAS1000000960

---

### Study ID

1000000960

---

### DARWIN EU® study

No

---

### Study countries

 Belgium

 France

-  Germany
  -  Ireland
  -  Israel
  -  Italy
  -  Netherlands
  -  Switzerland
  -  United Kingdom
- 

## Study status

Ongoing

## Contact details

### Study institution contact

Liana Barenbrug [liana.barenbrug@radboudumc.nl](mailto:liana.barenbrug@radboudumc.nl)

[Study contact](#)

[liana.barenbrug@radboudumc.nl](mailto:liana.barenbrug@radboudumc.nl)

### Primary lead investigator

Marleen van Gelder 0000-0003-4853-4434

[Primary lead investigator](#)

### ORCID number:

0000-0003-4853-4434

## Study timelines

### Date when funding contract was signed

Planned: 01/05/2025

Actual: 01/05/2025

---

### **Study start date**

Planned: 01/02/2026

Actual: 16/03/2026

---

### **Data analysis start date**

Planned: 01/02/2026

---

### **Date of final study report**

Planned: 01/02/2026

## Study protocol

[Protocol - IL17 23 pregnancy - v 02022026.pdf](#) (562.15 KB)

## Regulatory

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

No

---

### **Is the study required by a Risk Management Plan (RMP)?**

Not applicable

## Methodological aspects

### Study type

### Study type list

**Study topic:**

Disease /health condition  
Human medicinal product

---

**Study type:**

Non-interventional study

---

**Scope of the study:**

Other  
Safety study (incl. comparative)

**If 'other', further details on the scope of the study**

Safety during conception and pregnancy

**Data collection methods:**

Secondary use of data

---

**Study design:**

This study is a multinational cohort study utilizing multiple databases comprising prospectively collected cases and reference populations.

**Main study objective:**

Maternal exposures:

The primary aim of this study is to evaluate the risk of adverse pregnancy outcomes (spontaneous abortion, stillbirth, pregnancy termination), pregnancy complications (preeclampsia, gestational hypertension, gestational diabetes, and premature rupture of membranes [PROM]), and adverse neonatal outcomes (major birth defects, small for gestational age, low birth weight, preterm birth, infections) after maternal exposure to IL-17, IL-23, IL-2/23 inhibitors at conception and/or during pregnancy in the etiologically relevant time period for the outcome of interest.

Secondly, to provide more information directly relevant to clinical practice, we will stratify the primary analyses by underlying disease for which the IL-17, IL-23 or IL-12/23 inhibitor is prescribed (i.e. psoriasis, psoriatic arthritis, Crohn's disease, ulcerative colitis, and axial spondyloarthritis) to explore potential confounding by indication. Additionally, if the number of exposures allows, the results will be stratified per biologic type.

Paternal exposures:

In this study we aim to evaluate the risk of adverse pregnancy outcomes (spontaneous abortion, stillbirth, pregnancy termination), and adverse neonatal outcomes (major birth defects, small for gestational age, low birth weight, preterm birth,) after paternal exposure to IL-17, IL-23, IL-12/23 inhibitors at conception.

## Study Design

### **Non-interventional study design**

Cohort

## Study drug and medical condition

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

BIMEKIZUMAB

BRODALUMAB

GUSELKUMAB

IXEKIZUMAB

MIRIKIZUMAB

RISANKIZUMAB

SECUKINUMAB

TILDRAKIZUMAB

USTEKINUMAB

---

### **Anatomical Therapeutic Chemical (ATC) code**

(L04AC21) bimekizumab

bimekizumab

(L04AC12) brodalumab

brodalumab

(L04AC16) guselkumab

guselkumab

(L04AC13) ixekizumab

ixekizumab

(L04AC24) mirikizumab

mirikizumab

(L04AC18) risankizumab

risankizumab

(L04AC10) secukinumab

secukinumab

(L04AC17) tildrakizumab

tildrakizumab

(L04AC05) ustekinumab

ustekinumab

## **Population studied**

### **Short description of the study population**

Exposed group:

- Treatment with IL-17, IL-23 or IL-12/23 inhibitor: bimekizumab, brodalumab,

guselkumab, ixekizumab, mirikizumab, risankizumab, secukinumab, tildrakizumab, ustekinumab (independent of the indication for which the drug is prescribed).

o Maternal exposure: at least 3 months before date of LMP and/or during pregnancy.

o Paternal exposure: at least 3 months before conception.

Exposure is considered to occur if the time from one injection to the subsequent injection, according to the standard intervals for that specific interleukin inhibitor, falls within the period of interest.

- Type of IL-17, IL-23 or IL-12/23 inhibitor and timing of exposure at least per trimester is known.

Reference group

- For each IL-17, IL-23 or IL-12/23 inhibitor exposed case, at least two patients of the same sex and disease, without maternal or paternal exposure to IL-17, IL-23 or IL-12/23 inhibitors, matched for gestational age at enrolment (+/- two weeks) will be included.

---

### **Estimated number of subjects**

550

## Study design details

### **Setting**

Study period

Data until January 2026 will be collected, with an estimated delivery date cut off of October 1, 2025.

---

### **Data analysis plan**

## Duplicates

Identification of duplicates will be performed using a combination of details, including country of report, exposure year, maternal/paternal age, medication, dosage, duration of exposure, duration of pregnancy, pregnancy and neonatal outcomes. Identified duplicates will be excluded.

## Patient and treatment characteristics

Descriptive analyses will be performed to present maternal/paternal characteristics and treatment characteristics.

## Pregnancy and neonatal outcomes after maternal exposure

Birth defects will be classified by two independent researchers blinded for the exposure data, according to the European Network of Population-based Registries for the Epidemiological Surveillance of Congenital Anomalies (EUROCAT) ICD10-British Paediatric Association system (27). The assessment of major birth defects will be restricted to live births and pregnancy losses with confirmed outcomes after appropriate medical examination. Minor birth defects will not be classified due to the likelihood of underreporting. Descriptive analyses will be performed to show the occurrence of the major birth defects.

To estimate the risk on major birth defects the crude risk will be determined, by dividing the total number of infants or foetuses with birth defects by the sum of all live-born infants, plus the number of cases with known birth defects in stillbirths and terminated pregnancies.

To assess the association between exposure to IL-17, IL-23 or IL-12/23 inhibitors and the risk on pregnancy complications and adverse neonatal outcomes, modified Poisson regression will be applied, yielding relative risks (RR) with 95% confidence intervals (95% CI). This analysis will be adjusted for confounders using propensity score methods. Applicable confounders for each outcome will

be identified using Directed Acyclic Graphs (DAG).

Crude rates for spontaneous abortion and stillbirth will be calculate

## 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)

BELpREG: the Belgian pregnancy registry

---

### Data source(s), other

European Network of Teratology Information Services (ENTIS) centers, PRIDE Study (<https://pridestudy.nl/>), and BioCAPTURE registry (<https://biocapture.nl/?lang=en>).

---

### Data sources (types)

[Disease registry](#)

[Other](#)

[Pregnancy registry](#)

---

### Data sources (types), other

## 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