

# Impact of EU label changes for medicinal products containing methotrexate for weekly administration: risk awareness and adherence, A survey study

**First published:** 22/12/2021

**Last updated:** 27/03/2024

Study

Finalised

## Administrative details

### EU PAS number

EUPAS44827

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### Study ID

50306

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### DARWIN EU® study

No

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### Study countries

 France

 Germany

 Greece

 Poland

 Sweden

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## **Study description**

MTX is authorised in the EU as a chemotherapeutic agent in multiple oncology indications and the low-dose MTX variant is also used as disease-modifying antirheumatic drugs (DMARDs). MTX administration cycle depends on the type of indication being treated, with a weekly low-dose schedule for autoimmune diseases (e.g. rheumatoid arthritis, juvenile idiopathic arthritis, psoriasis, psoriatic arthritis, steroid sparing adjunctive therapy in Crohn's disease, acute lymphocytic leukaemia in children) and cycles of different numbers of days with a daily dosing schedule for oncology indications. Inadvertent consumption of prescribed MTX daily doses instead of a single once a week dose, can cause serious overdose issue, sometimes fatal. In 2019, a referral procedure based on pharmacovigilance data concluded that further risk minimisation measures would be required for oral and parenteral MTX containing products, in order to avoid incorrect administration schedules, i.e. inadvertent MTX overdose due to daily use instead of weekly. The survey will measure risk awareness and knowledge amongst healthcare professionals (HCPs) (prescribers and pharmacists) involved in prescribing and dispensing and user of oral and parenteral authorised MTX in the EU following the implementation of the 2019 measures to avoid incorrect administration.

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## **Study status**

Finalised

## **Research institutions and networks**

### **Institutions**

**IQVIA**

 United Kingdom

**First published:** 12/11/2021

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**Institution**

**Non-Pharmaceutical company**

**ENCePP partner**

## Contact details

### Study institution contact

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**Study contact**

[PAS\\_registrations@iqvia.com](mailto:PAS_registrations@iqvia.com)

### Primary lead investigator

Massoud Toussi

**Primary lead investigator**

## Study timelines

### Date when funding contract was signed

Actual: 10/05/2021

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### Study start date

Planned: 01/02/2022

Actual: 25/02/2022

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### **Data analysis start date**

Planned: 19/04/2022

Actual: 19/04/2022

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

Planned: 12/09/2022

Actual: 04/10/2022

## Sources of funding

- EMA

## Study protocol

[Methotrexate Protocol\\_v1.0.pdf](#) (880.87 KB)

[SC02 EMA2018\\_19\\_PE\\_Methotrexate Protocol\\_v2.0\\_21 Feb 2022\\_Signed.pdf](#)  
(1.27 MB)

## Regulatory

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

Yes

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

Not applicable

## Methodological aspects

### Study type

### Study type list

**Study topic:**

Human medicinal product

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**Study type:**

Non-interventional study

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**Scope of the study:**

Effectiveness study (incl. comparative)

**Data collection methods:**

Primary data collection

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**Main study objective:**

The overall objective of the study is to evaluate the impact of these actions taken for MTX-containing medicinal products following the 2019 referral procedure.

## Study Design

**Non-interventional study design**

Cross-sectional

Other

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**Non-interventional study design, other**

Multinational, and multichannel survey

## Study drug and medical condition

**Anatomical Therapeutic Chemical (ATC) code**

(L04AX03) methotrexate

methotrexate

## Population studied

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

The study population included healthcare professionals who had prescribed a weekly dose of methotrexate (MTX), pharmacists who had dispensed a weekly dose of MTX, and patients who had used a weekly dose of MTX in 5 European countries (France, Greece, Germany, Poland, and Sweden) for the period of 25 February 2022 to 11 April 2022.

#### Inclusion Criteria:

- For prescriber questionnaire: Prescribers who have prescribed MTX in a single low dose once a week for indications that require weekly dosing in the past 3 months
- For pharmacist questionnaire: Pharmacists who have dispensed MTX in a single low dose once a week for indications that require weekly dosing in the past 3 months
- For patient questionnaire: Patients who have been treated with a single low dose once a week for indications that require weekly dosing in the past 3 months

#### Exclusion Criteria:

- Prescribers, pharmacists, or patients who declare having a conflict of interest with the survey (i.e. participants employed by regulatory bodies, pharmaceutical industries)
  - Prescribers, pharmacists, or patients who do not provide consent for participating in the survey
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## **Age groups**

- Adults (18 to < 46 years)
  - Adults (46 to < 65 years)
  - Adults (65 to < 75 years)
  - Adults (75 to < 85 years)
  - Adults (85 years and over)
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## **Estimated number of subjects**

450

# Study design details

## **Outcomes**

For prescriber: receipt and awareness of the DHPC and EMs for HCPs awareness of the patient card and the knowledge of the risks of overdose due MTX weekly use. For pharmacist, awareness of the patient card and the visual reminder of MTX, For patient: awareness and knowledge of the elements introduced to avoid incorrect administration for MTX and adherence to marking the day of intake of MTX.

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## **Data analysis plan**

The statistical results of the selected countries will be presented in the same report, overall and per country. Continuous variables will be described by their number (of valid cases and missing values), mean, standard deviation, and median, first quantile (Q1), third quantile (Q3), minimum and maximum. Categorical variables will be described as the total number and relative percentage per category. These will be the percentage per category. In case of multiple-choice questions, the frequency of each option provided by the participants will be reported in the statistical results. Different combinations of

the answers provided will not be considered. CIs of 95% will be evaluated, when relevant. the results will be weighted according to the real proportion of prescribers, pharmacists, and patients who in each country in order to accurately reflect the population that the survey seeks to measure.

## Documents

### Study results

[Methotrexate report - SC02 EMA\\_2018\\_19\\_PE\\_MTX\\_v 2.0\\_20221213.pdf](#) (1.69 MB)

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### Study, other information

[Methotrexate synopsis.pdf](#) (125.49 KB)

## 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 sources (types)

[Other](#)

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### Data sources (types), other

The survey is a primary data collection conducted through 3 questionnaires administered by web: A prescriber questionnaire, A pharmacist questionnaire, A patient questionnaire

## Use of a Common Data Model (CDM)

### **CDM mapping**

No

## Data quality specifications

### **Check conformance**

Unknown

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### **Check completeness**

Unknown

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### **Check stability**

Unknown

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### **Check logical consistency**

Unknown

## Data characterisation

### **Data characterisation conducted**

No