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

Study ID

50306

DARWIN EU® study

No

Study countries

- [ ] France
- [ ] Germany
- [ ] Greece

- [ ] Poland
- [ ] Sweden

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.

Study status

Finalised

Research institutions and networks

Institutions

IQVIA

United Kingdom

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Institution | Non-Pharmaceutical company | ENCePP partner

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Massoud Toussi

Primary lead investigator

Study timelines

Date when funding contract was signed

Actual: 10/05/2021

Study start date

Planned: 01/02/2022

Actual: 25/02/2022

Data analysis start date
Planned: 19/04/2022

Actual: 19/04/2022

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

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:

Effectiveness study (incl. comparative)

Data collection methods:

Primary data collection

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

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

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)

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.

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)

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

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

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No